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FINAL REPORT

NAS 9-17428 - EL 04-85-GC1

A Study To Define A Set of Requirements
For Cleansing Agents For Use in the Space Station
Whole Body Shower.

October 29, 1985



(NASA-CR-171910) A STUDY TO DEFINE A SET OF
REQUIREMENTS FOR CLEANSING AGENTS FOR USE IN
THE SPACE STATION WHOLE BODY SHOWER Final
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ECONOMICS LABORATORY, INC.
Osborn Building
St. Paul, Minnesota 55102

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INTRODUCTION

The purpose of this contract is to assist NASA engineers in defining a set of requirements for a whole body cleansing agent to be used in the Space Station Whole Body Shower System. In addition, cleansing agent candidates are to be identified that are likely to satisfy requirements defined in the first part of the study. It is understood that the main reason for having a Whole Body Shower is to satisfy the physiological, psychological and social needs of the crew throughout the duration of duty in the Space Station. The cleansing agent must also be compatible with the vortex water/gas separator and the water reclamation system. To accomplish these goals the study was divided into six tasks.

These tasks are as follows:

1. Task One: Survey literature and unpublished information to ascertain state-of-the-art in Whole Body Shower cleansing and the potential impacts of extended use of WBS cleansing agents in a microgravity environment. Integrate cleansing agent and microgravity literature to develop an understanding of using cleansing agents in a microgravity environment.
2. Task Two: Characterize human physiological, psychological and sociological requirements of cleansing and develop human aspect criteria for cleansing agents operating in a microgravity environment.
3. Task Three: Characterize spacecraft equipment environmental needs and develop microgravity equipment environment criteria for cleansing agents.
4. Task Four: Integrate human and equipment criteria developed in Tasks Two and Three and develop a preliminary list of cleansing agent candidates. Develop a matrix showing correlation between candidate cleansing agent performance and cleansing agent criteria. Identify areas where existing cleansing agents do not meet criteria.

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5. Task Five: Review established test procedures of extended use of cleansing agents on humans and equipment. Develop new protocols where existing testing procedures cannot predict the suitability of meeting any of the new suitability criteria developed in Tasks Two and Three.
6. Task Six: Prepare a summary report of the evaluation process, development of suitability criteria and listing of candidate cleansing agents, accompanied by an annotated bibliography of pertinent cleansing agents and microgravity literature.

FINAL PROGRESS REPORT
NASA Contract NAS9-17428
EL #04-85-GC1 - Effective date: July 1, 1985

Contract: STUDY TO DEFINE A SET OF REQUIREMENTS FOR CLEANSING
 AGENTS FOR USE IN THE SPACE STATION WHOLE BODY
 SHOWER.

This contract had two general requirements. These were to assist NASA in defining a set of requirements for a cleansing agent and to suggest likely cleansing agent candidates.

I. DEFINITION OF A SET OF REQUIREMENTS FOR A CLEANSING AGENT
 TO BE USED IN THE WHOLE BODY SHOWER (WBS) SYSTEM FOR THE
 SPACE STATION.

Task 1: Survey cleansing agent and microgravity literature -
characterize information base.

An outline of subjects was compiled and was used to generate key words for the literature searches. This outline is as follows:

A. Human Compatibility

1. Skin irritability of soaps and surfactants
2. Eye irritation of soaps and surfactants
3. Dandruff causes and control
4. Skin defatting
5. Shampoo testing criteria
6. Sanitization from soaps and surfactants
7. Allergic reactions from soaps and surfactants
8. Dermatitis

B. Equipment Compatibility

1. Water treatment
2. Shower and separator equipment
3. Corrosivity toward equipment
4. Filming on shower walls
5. Compatibility with shower disinfectant

C. Human Comfort and Feel

1. Extended use effect
2. Sociological requirements
3. Residual odor on body
4. Odor of cleansing agent
5. Rinse-ability and residue of cleansing agent on skin and hair
6. Dandruff and testing for skin bacteria, flora or micro-flora

D. Applicators of Cleansing Agent

1. Sponge
2. Wash cloth
3. Brush
4. Others

Using this outline, EL's Information Center completed two types of searches. The first was a manual search of internal documents and book collections. The second was a computer search of Dialogue's Readable Data Service and some of the NASA RECON databases. As a result of these searches, a total of 170 references were sourced from Dialogue and fifteen references ordered as a result of the NASA RECON search.

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Databases searched during the life of the contract from Dialogue were:

<u>DATABASE NAME AND NUMBER</u>	<u>YEAR</u>
CHEMICAL ABSTRACTS 308, 309, 320, 310, 311	1967-1985
MEDLINE 152, 153, 154	1966-1985
EXCERPTA MEDICA 173, 172, 72	1974-1985
NTIS 6	1964-1985
DISSERTATIONS ABSTRACTS 35	1861-1985
SCISEARCH 186, 94, 87, 34	1974-1985
AEROSPACE 108	1962-1985
SOVIET SCIENCE & TECHNOLOGY 270	1975-1985
CONFERENCE PAPERS INDEX 77	1973-1985
LIFE SCIENCES 76	1978-1985
WORLD PATENTS 350, 351	1963-1985
NURSING & ALLIED HEALTH 218	1983-1985

A list of references obtained is shown in Appendix A. Where appropriate, comments are made that summarize relevant conclusions drawn from the reference.

Task 2: Analyze Human Physiological and Psychological Needs and Develop Human Cleansing Agent Criteria

The literature taken from the Task 1 search was reviewed and analyzed to assist in developing human cleansing agent needs in a microgravity environment. Observations falling under the Task 2 category are:

A. Microgravity considerations

1. Microgravity will make rinsing from the hair and eyes more difficult.
 - a. High viscosity cleansing agents are generally more irritating to the eyes. This may be due to difficulty of removal from the eyes by blinking.
 - b. Higher pH products, i. e. 7.0-8.5 are more irritating to the eye. pH 5.0-6.0 is preferred. Products with a pH similar to that of the skin produce minimal skin microflora change. Unpublished data shows a change in the number and type of microflora in the axillary vault during normal use of standard commercial products that produced a transient change in vault pH.

B. Cleansing Considerations

1. Since soft water will be used for rinsing, fatty acid soaps which are very poor rinsers in soft and deionized water, are not recommended.
2. A properly formulated shampoo will function satisfactorily as a body cleanser so the focus of the project should be on shampoo properties. Economics Laboratory's unpublished consumer test results indicate this to be true.
3. A review of numerous articles on shampoo formulations states that proper foam is the most important property of a shampoo because the consumer equates foam with soil removal, i. e. a clean and invigorated feeling. An effective foam includes volume, stability and foam structure.

A no-foam cleansing agent SED 48101653-501 was obtained from NASA and evaluated. Detailed experimental results are listed in Section II. The major conclusion noted is that the no-foam property leads to excessive use. This result was confirmed by

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NASA personnel, who found that the no-foam property was disliked and leads to excessive use. (15-25 grams per shower).

To test the hypothesis that high foam results in lower cleansing agent use, several commonly used high-foaming shampoo ingredients were evaluated using a 1 gallon water delivery system.

Procedure, results and conclusions are shown below:

Two 0.25 gallon/minute distilled water shower delivery systems were constructed. The first was a prototype 1 gallon water delivery system and the 2nd consisted of a demand activated 12 VDC water pump (Shur Flo Model No. 200-219-39 made for recreational vehicle), using a spraying systems nozzle 1/8 CG 3002.5. (See Figure 1)

The 1 gallon system was used to subjectively determine whether various surfactants could be rinsed off the hair and body with one gallon of distilled water. The test consisted of a series of showers using different surfactant raw materials. The amount of surfactant required and general subjective observations were made.

Date of shower, product used, amount used and general comments are shown below.

<u>DATE</u>	<u>PRODUCT</u>	<u>AMT. USED</u>	<u>COMMENTS</u>
7/30/85	Hamposil L30	2.7g	Lathered well as shampoo but decayed in time. Lather on body adequate.
7/31/85	Hamposil L30	1.9g	Somewhat low on foam.
8/1/85	Hamposil L30	4.7g	Fairly adequate on lathering.
8/2/85	Hamposil L30	4.2g	Adequate lathering on hair, somewhat low on body.
8/5/85	Hamposil L30	4.6g	Same as above.
8/6/85	Sodium Lauryl Sulfate	2.0g	Adequate lathering on hair and body.
8/7/85	Sodium Lauryl Sulfate	2.5g	Adequate lathering on hair and body.
8/8/85	Sodium Lauryl Sulfate	3.1g	Adequate lathering on hair and body.
8/10/85	Sodium Lauryl Sulfate	3.4g	Adequate lathering on hair and body.
8/11/85	Sodium Lauryl Sulfate	2.5g	Adequate lathering on hair and body.
8/12/85	Ammonium Lauryl Sulfate	2.9g	Adequate lathering on hair and body.
8/13/85	Magnesium Lauryl Sulfate	3.7g	Lather adequate on hair and body.
8/14/85	Alcohol Ethoxy Sulfate (Neodol 25-S3)		Good lathering on hair and body, skin felt slightly dry.
8/17/85	Ammonium Lauryl Ether Sulfate	3.0g	Used too much product. Lather very good on hair and body. Rinsed well Skin felt good.
8/18/85	Ammonium Lauryl Ether Sulfate	2.3g	Still used too much. Comments same as above.
8/19/85	Miranol C3M Conc.	2.0g	Lather OK on hair but inadequate for body.
8/21/85	Miranol C2M Conc.	2.7g	Lather OK on hair, barely adequate for body.

- a. All products tested rinsed off adequately using one gallon of distilled water for the total shower.
- b. When lathering was too copious on hair about 1/3 or more of the water was required to rinse the hair.
- c. Eye smarting as such was not reported and did not appear to be a problem. The problem was avoided by keeping the eyes closed for 30 seconds or so after washing the face. However, in a zero gravity situation this could be a problem and it would be necessary to deliberately place some product or raw materials into the eyes to objectively test for this property.
- d. The use of a sponge is believed to be good in removing dead cells and leaving the skin with a good feeling.
- e. In all cases, it is believed that some rubbing action with the free hand while rinsing is advisable to obtain good rinsing.
- f. The area between the shoulder blade is not easily accessible and further consideration might be given to this potential problem.
- g. The amount of surfactants used in the test is small when contrasted to the amount of NASA non-foam cleaner reported last month. It indicates that foam is unconsciously used as a criteria for 'knowing' how much cleaner is to be used. Thus, a premeasured one-use package might be advisable. This will prevent over application and resulting problems which might occur in the water recovery system when cleansing agents are over-used.

4. Shampoo testing criteria can be divided up into two types of test results. Tests whose results are measured objectively and those where results are measured subjectively. The first category contains most safety type testing procedures listed in Task 5. The second category consists of tests to measure the success of the cleansing agent in satisfying psychological needs. These points are listed below and are usually evaluated by an experienced operator doing half head tests. These are as follows:
 - a. Ease of spreading
 - b. Lathering power
 - c. Efficient soil removal
 - d. Ease of rinsing
 - e. Ease of combing wet hair
 - f. Luster of hair
 - g. Hair must smell clean and fresh
 - h. Ease of combing and setting of dry hair
 - i. Speed of drying
 - j. Feel on hands
5. A preservative in the cleansing agent is acceptable, but an antimicrobial to alter body flora is not.
6. It is recommended using only proven shampoo raw materials well known in the art as part of the cleansing agent formulation.

Task 3: Analyze Equipment Environmental Needs and Develop
Equipment Cleansing Agent Criteria.

The following publications were received from NASA and all were reviewed:

1. Zero-G Whole Body Shower Development Program Test Plan - 82-273.
2. Space Station Environmental Control and Life Support System Architecture: Centralized vs. Distributor.
3. Extended Mission Life Support Systems, June 1981
4. Space Station Prototype Advanced Life Support System Hardware Testing
5. Atmosphere Revitalization in the Space Station Prototype.
6. Integrated Atmosphere Revitalization System Description and Test Results.
7. Solid Polymer Electrolyte (SPE) Water Electrolysis
8. Development Status of Preprototype Water Electrolysis System.
9. Development Status of a Preprototype Water Electrolysis Subsystem.
10. Electrochemical Depolarized CO2 Concentrator (EPD).
11. Development of a Three-man Prototype CO2 Collection Subsystem for Spacecraft Application.
12. Regenerable CO2 Collection for Spacecraft Application.
13. Solid Amine Water Desorbed (SAWD) CO2 Concentrator.
14. Development of Solid Amine CO2 Control Systems for Extended Duration Missions.
15. Space Station Prototype Sabatier Reactor Design Verification Testing.

16. Design of A Spacecraft Containment Control System.
17. Carbon Formation Reactor.
18. Development of a Three-Man Prototype Independent Air Revitalization Subsystem.
19. Integrated Water Management System Description and Test Results.
20. Development of Water Quality Monitor For Spacecraft Application.
21. Development of an Advanced Combined Iodine Dispenser/detector.
22. Design, Fabrication and Acceptance Testing of a Zero Gravity Whole Body Shower
23. Hyperfiltration Wash Waster Recovery Subsystem - Design and Test Results.
24. Extended Testing Of Compression Distillation.
25. Design and Parametric Testing of the Space Station Prototype Integrated Vapor Compression Distillation Water Recovery Module.
26. Improved Waste Water Vapor Compression Distillation Technology.
27. Application of Improved Technology to a Preprototype Vapor Compression Distillation Water Recovery Subsystem.
28. A Thermoelectric Integrated Membrane Evaporation System.
29. Development of a Preprototype Thermoelectric Integrated Membrane Evaporator Subsystem for Water Recovery.
30. Thermoelectric Integrated Membrane Evaporator Water Recovery Technology
31. Urine Pretreatment for Waste Water Processing Systems.
32. Thermoelectric Integrated Membrane Evaporation Subsystem Operational Improvements.

33. Design, Development and Operation of a Zero Gravity Shower.
34. Final Report - Zero Gravity Whole Body Shower Tests
35. Centrifugal Shower Separator of the Orbiter Workshop Habitability Support Station.
36. Recommended Tentative Standards for Wash Water for Manned Spacecraft.
37. Water Quality Standards for Long Duration Manned Space Missions.
38. Procedure Development for Water Analysis.
39. Final Report - Spacecraft Sanitation Agent Development.
40. Potable Water Standards for Aerospace Systems.
41. Technology Development for a Zero Gravity Whole Body Shower.
42. Evaluation of Proposed Skylab and SSP Soap Products.
43. Evaluation of a Multifiltration Water Reclamation Subsystem to Reclaim Domestic Clothes Wash Water.
44. Final Report - Design, Fabrication and Acceptance Testing of a Zero Gravity Whole Body Shower.
45. Final Report on Prototype Wash Water Waste Renovation System.
46. Final Report on Prototype Wash Water Renovation System Integration with Government Furnished Wash Fixture.

OBSERVATIONS THAT HAVE BEEN MADE AS A RESULT OF THIS LITERATURE REVIEW ARE:

1. As a result of the August 6-7, 1985 meeting with NASA, the type of water reclamation system is not yet determined and ferric chloride precipitation is not preferred.
2. NASA would like to pre-treat waste water in some manner to remove gross soils.
3. Polyethylene or coated metals will not be used in any water reclamation systems. Materials of construction incorporated into the latest design of the wash water recovery system will be stainless steel type 316, titanium,

and Teflon. If these are incorporated into the final design there will be no corrosion problems associated with the Whole Body Shower Cleansing Agent.

4. The system will use deionized water. Particular attention must be paid to rinse-ability. For example, soaps become very difficult to rinse in deionized water.
5. To simplify housecleaning, the cleansing agent should not leave a film on the shower.
6. The vortex air/liquid separator will not function properly with high foaming solutions. However, it has been documented that cleansing agent consumption increases drastically if the foam levels are low. In addition, one's perception of cleanliness is low if foam levels are also low.

A method of defoaming this solution should be incorporated between the shower stall and the vortex air/liquid separator, thus allowing the use of a high foaming Whole Body Cleansing Agent.

7. Defoaming of cleansing agent raw material ingredients has been evaluated. Detailed results are given in Section II of this report. The conclusion from the preliminary investigation is that high foaming cleansing agent solutions can be effectively defoamed with low levels (less than 10 ppm) of defoamer. The concentration is based upon the volume of wash solution. This is particularly encouraging because this permits use of normal ingredients used for whole body cleansing agents which will provide a better feeling shower.
8. Commercial shampoos contain many unnecessary ingredients (if liquid) because their function is to provide proper form, fragrance and appearance. (See Table #2) These ingredients complicate water reclamation.
9. A concentrated cleaner is recommended using only 2-4 ingredients. This simplifies water reclamation.
10. A concentrate is recommended to eliminate unnecessary weight.
11. The microgravity shower film (obtained from NASA, Zero G Shower 1972 KC 135 Research) shows that water does not drip or run off the body. This reveals two potential problems. The first is that it will be more difficult to rinse the cleansing agent from the hair and body - particularly the

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hair. The second is that special attention has to be paid to eye irritation because it will be difficult to rinse cleansing agent from the eyes.

Task 4: Integrate Human and Equipment Cleansing Agent Criteria and Develop a Matrix Comparing Candidate Cleansing Agent Performance with Criteria.

Three conflicts between Task 2 and Task 3 observations have been identified. These are as follows:

1. Observation B-3 from Task 2 requires a high foam cleansing agent to assure the physiological, psychological and social needs of the crew members. This is the main reason for having a Whole Body Shower in the Space Station, and is clearly the number one priority. It is in conflict with Observation 6 from Task 3 where the vortex air/liquid separator does not function properly with high foam solutions. This conflict appears to be irreconcilable unless the system is designed to provide high foam during use and low or no-foam when the waste water reaches the vortex separator.

Our research demonstrates that such a system can be developed using a suitable defoamer. Details are provided in Section II of this report.

2. Observation B-2 from Task 2 requires a suitable shampoo. This requirement conflicts with Observation 8 from Task 3 which notes that commercial shampoos contain unnecessary ingredients that complicate water reclamation. This problem is lessened if a special product is formulated in concentrated form using only 2-4 ingredients.
3. Observation B-2 from Task 2 is also in conflict with Observation 9 of Task 3 which requires an extremely mild cleansing agent to avoid eye irritation. Normal shampoos are formulated with inexpensive raw material cost constraints. Less expensive primary shampoo ingredients usually cause eye irritation or pain.

Because raw material cost constraints are not a major factor in developing a space station cleansing agent, this conflict can be resolved by formulating a very mild cleansing agent.

The cleansing agent candidate and candidate defoamer presented in Section II are likely to meet the human and equipment criteria that have been established. The candidates take into account the three conflicts identified. A matrix has not been constructed because its purpose was to assign values to conflicting criteria and to estimate which candidates have the highest total values vs. all criteria. All candidates presented would have the

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same value, so a matrix serves no purpose. A matrix ordering candidates as best satisfying performance criteria should be completed when the Task 5 protocols listed in this report are completed.

Task 5: Review Existing Test Protocols and Develop New Test Protocols.

The results of the literature search completed in Task 1 and the listing of cleansing agent criteria and observations in Task 2 and 3 dictate whether existing test protocols are appropriate or whether revisions are necessary. There are two types of test protocols to consider. These are toxicity testing and cleansing agent performance testing.

A. Toxicity Testing - the following test procedures and test results are specified.

1. Acute oral toxicity (LD50) - concentration that produces death in 50% or more of the test animals within 14 days.

Procedure - HG-acute-oral - October 1984 - Office of Pesticides and Toxic Substances. United States Environmental Protection Agency.

Acceptable result - no deaths at 5 grams per kilogram. This is the limit test.

Species:	10 wh. rats (5M-5F)
Dose:	Limit test: 5 g/kg of body weight
Defined:	3 dose level (10 rats ea)
Observation:	14 days
Interpretation:	LD50 of .05g/kg or less = highly toxic
	LD50 of more than .05g/kg - 5g/kg =
	Toxic
	LD50 of more than 5g/kg = not toxic

2. Primary skin irritation
Procedure - 16 Code of Federal Regulations, 1500.41
Acceptable result - score of 5 or less.

Species: 6 rabbits
Dose: 0.5mls or 0.5g of solid (in liquid)
Exp. method: 2 - 1"x1" shaved skin sites (1 abraded)
Exp. Time: 24 hours
Observation: 24,48 & 72 hrs or up to 3 wks.
Calculation: Average readings for 6 rabbits
Add values at 24 & 72 hrs for both sites
for erythema & edema (total: 8
readings) & divide 4 = primary skin
irritation score.

Interpretation: Score of 5 or less - not primary
irritant
Score of more than 5, product is a
primary skin irritant.
Irreversible damage - corrosive

3. Primary eye irritation
Procedure - 16 Code of Federal Regulations, 1500.42
Acceptable result - legal definition of non-
irritating.

Species: 6 rabbits
Dose: 0.1ml (for solids 100 mg) in 1 eye.
(2nd eye for control)
Observations: 24,48,72 hours
(Eye may be washed after 24 hours)
Positive if: Cornea is ulcerated or opaque, iris is
inflamed, conjunctivis is red, swollen
or invested.
Interpretation: 4 or more positive, product is a PRIMARY
eye irritant.
1 positive, test is negative, product is
not an irritant.
2 or 3 positive, rerun with a new set of
animals.
Second test is positive for 3 or more,
test is positive.
2nd test is positive for 1 or 2, then
repeat.
If 3rd test has 1 positive, then test is
positive.
If damage is irreversible after 21 days,
product is corrosive.

4. Dermal Sensitization
Procedure: This procedure is specified in Appendix B.
Acceptable result: Not classified as a primary sensitizer.
5. Clinical eye irritation
This procedure is run on human subjects and is to determine whether the candidate exhibits eye smarting or pain. This procedure is given as Appendix C.
Acceptable results: Clinically acceptable result.
6. Acute dermal toxicity and acute inhalation toxicity.

These tests are not recommended because in the former case generally recognized shampoo ingredients will be used, and in the second case, the procedure is valid only for aerosol type products.

B. Performance Testing

1. Ross-Miles Foam Testing

Procedure - ASTM D 1173

2. Hair tress testing - the procedure for tress testing is as follows:

- a. One gram of hair 5 inches or longer (the tress) will be washed using the test product and then rinsed.
- b. The tress will be combed while wet and evaluated (ease of combing, luster, product residue or other noticeable factors).
- c. The tress will be allowed to air dry. It will then be evaluated for appearance, ease of combing product residue or other noticeable factors.
- d. This will be repeated 20 times to see if any long term effects will be seen.
- e. This will be repeated using artificial sebum treated hair tresses (on new tresses).

The formula for artificial sebum is given in the following article: Spangler, Cross, and Schoafoma, Journal of the American Oil Chemists Society, 42 723 (1965). Formulation is as follows:

<u>INGREDIENT</u>	<u>PERCENT</u>
Linoleic Acid	5%
Olive Oil	20%
Coconut Oil	15%
Palmitic Acid	10%
Stearic Acid	5%
Oleic Acid	10%
Paraffin Wax	10%
Squalene	5%
Spermaceti	15%
Cholesterol	5%

The artificial sebum is applied to the hair tresses at a concentration of either 2% or 10% in Hexane.

3. Half-head Testing

This procedure is to be modified to use deionized water and special attention is to be paid to rinseability. The procedure is listed in Appendix D. Acceptable result: Result acceptable to qualified clinician.

4. Microgravity foam test

It is recommended that NASA determine under microgravity conditions whether foam presents unforeseen difficulties.

II. ASSISTING NASA IN THE SELECTION OF VARIOUS CLEANSING AGENT CANDIDATES WHICH SATISFY REQUIREMENTS DEFINED IN THE FIRST PART OF THE STUDY

A. Cleansing Agent Evaluations

Evaluations were carried out at Economics Laboratory and NASA to determine whether common shampoo ingredients would function properly in the vortex air/liquid separator.

A male and female showered with a sufficient quantity of liquid cleansing agent and rinsed with a minimum of water to determine how much cleansing agent is required to do a sufficient job. The results were 2.9 and 4.9 grams respectively. Based upon this result several surfactant systems were sent to NASA for testing for foam in the air/water separator equipment. Results of that study and of Ross Miles Foam Tests are listed in Table #1 (attached).

The conclusion from this study is that normal high foaming shampoo ingredients will not work in the vortex separator unless they are defoamed. Further, the result with Ivory shampoo indicates that it is likely that all commercial products as formulated will fail unless they are defoamed.

Six modern commercial shampoos were purchased, the pH recorded, and ingredients reviewed. Results are given in Table #2 (attached). All of these commercial shampoos contain anionic syndets as the primary surfactant, use other ingredients to increase lather and to condition hair, have an acid pH, and use a preservative because it is well known that liquid shampoos containing sufficient water require preservation. All contain over ten ingredients which will tax the water reclamation system.

The shower soap being used now by NASA has been evaluated. This is non-foam soap SED 48101653-501. This product was indeed non-foaming. No lather obtained during shampooing the hair or washing the body.

Major problem encountered was in knowing when enough product was applied to the hair and body. Normally, when an insufficient amount of foaming shampoo is used all of the surfactant combines with the soil (body oils) and none is left to cause lathering; when sufficient amount or slight excess is applied to the hair lather forms. With the non-foaming product there is a tendency to over-use the product since the bather can not see any lather forming. This in turn may cause an excessive degreasing of the scalp or skin and cause itching and perhaps even scaling and/or dandruff as experienced by one female astronaut.

Using one-gallon shower (distilled water) the following application of the non-foam soap was recorded:

7/26/85	10.6g
7/27/85	18.4g
7/28/85	19.5g
7/29/85	13.0g

Some itching of the scalp, shoulder blades and waist area was experienced after the showers with non-foaming soap product.

In contrast to the above application, other product usege under same showering conditions were as follows:

Miranol JEM	6.3g
Igepon TC-42	6.3g
Showermate	4.2g
Ammonium Lauryl Sulfate - 30%	2.7g
Ammonium Lauryl Sulfate - 30%	4.7g

Major conclusions have been drawn from our studies of cleansing agents:

1. Fatty acid soaps should not be considered for the following reasons:
 - a. Calcium defoaming is possible but will likely cause shower stall filming which will cause housekeeping problems and potentially harbor invisible bacteria.
 - b. No shampoos are alkaline anymore. Alkalinity causes roughening of the scales of the hair cuticle, thus giving a dull appearance and potentially damaging to the scalp.
 - c. Alkanolamine soaps, which are neutral, are not used because of the potential to form nitrosamine.
 - d. Fatty acid soaps do not rinse easily in deionized water. As a result, ferric chloride precipitation is not a viable water pretreatment method for water reclamation.
2. Some foam is necessary for proper feel for the following reasons:
 - a. Foam is associated with efficacy.

- b. Foam prevents over use of the cleansing agent.
- c. Foam itself assists in greasy soil removal and prevents soil redeposition by holding soil particles in the foam matrix.
- d. Foam serves as a visual indicator that that part of the body has been cleaned.

B. Specifications General

The specifications for the sponge towelette that have been evaluated by NASA are:

Identity:

Polyether sponge foam grade 39XX
Supplier: General Foam Corp,
West 100 Century Rd
Paramus, New Jersey 07652
Phone: 201 - 262-7500

C. Antifoam Evaluations

Evaluations of several anti-foam preparations were completed with the goal of identifying a material that provides sufficient defoaming of high foam anionic surfactants using very little defoamer. Results follow:

<u>SUPPLIER</u>	<u>ANTIFOAM</u>	<u>RESULT</u>
Dow Corning	544	No effect below 500 ppm
Dow Corning	Q13563	No effect below 500 ppm
Dow Corning	Cationic 929	No effect below 500 ppm
Dow Corning	1107 fluid	No effect below 500 ppm
Dow Corning	200 fluid	No effect below 500 ppm
Dow Corning	536 Fluid	Effective @ 10 ppm
Dow Corning	Q32168	No effect below 500 ppm
Gen'l Electric	SF96-50	No effect below 500 ppm

The results indicate that 536 Fluid is an effective defoamer at low concentrations.

D. Foam Testing

Ross Miles foam tests were carried out to assess the foam effect of a hair conditioner and an eye irritation reduction ingredient. These are Lecipur 95 (lecithin) and sorbitan monooleate (Span 80) respectively. Both ingredients were found to increase foam. Moreover, the

lower foaming the anionic, the more of an increase. High foamers were affected only slightly.

E. Cleansing Agent Candidate Systems

1. Cleansing Agents

Seven cleansing agent candidate formulations are provided. All formulations use common shampoo ingredients. All are adjusted to pH 5-6 with hydrochloric acid. All contain a primary anionic surfactant with 1-3 other ingredients added to improve conditioning and to make less irritating. None of the formulas contain a preservative.

If these are concentrated to have low enough water activity there is no need for a preservative. However, if used at 20%, then a preservative system would be necessary. The no-foam candidate we received from NASA has begun to break down after 3 months. The container is bulging and the product smells quite bad. Either this product does not contain a preservative or the preservative is inadequate. This type of breakdown is common for an unpreserved aqueous surfactant system.

Ross Miles foam results are listed for each candidate, and compared to the NASA Low Foam Product and Prell.

These results indicate that none of the candidates will pass the vortex separator test without being defoamed. However, they provide sufficient foam to be perceived as suitable whole body cleansing agents.

The list of candidates are shown on the following page.

WHOLE BODY SHOWER FORMULAS - ROSS-MILES FOAM TEST

<u>RAW MATERIAL</u>	<u>A</u>	<u>B</u>	<u>C</u>	<u>D</u>	<u>E</u>	<u>F</u>	<u>G</u>	NASA <u>FMLA</u>	<u>PREL</u>
Water, Distilled	27.08	60.42	25.33	42.00	57.50	54.50	80.00		
Sod. Lauryl Sulfate (30% Active) (Stepanol WAC)	66.67	-	-	-	-	-	-		
Sod. Lauryl Ether Sulfate (60% Active) (Steol CS-460)	-	33.33	-	-	-	-	-		
Sod. Lauryl Sarcosinate (30% Active) (Hamposyl L-30)	-	-	66.67	-	-	-	-		
Sod. Alpha Olefin Sulfonate (40% Active) (Bioterge AS-40)	-	-	-	50.00	-	-	-		
Lecithin (Lecipur 95F)	0.25	0.25	-	-	-	-	-		
Cocoyl Amide Alkylamine Oxide (50% Active) (Textamine Oxide CA)	-	-	2.00	2.00	-	-			
Polymer JR-30M	1.00	1.00	1.00	1.00	-	-	-		
Tween 20	-	-	-	-	5.00	-	-		
Miranol C2M-SF Conc. (40% Active)	5.00	5.00	5.00	5.00	37.50	-	-		
Monamid 150-ADY	-	-	-	-	-	3.00	3.00		
Monamate CPA-40 (40% Active)	-	-	-	-	-	42.50	-		
Monamine 779	-	-	-	-	-	-	17.00		
Raw materials are 100% active except as noted.									
Total % Solids	23.25	23.25	24.00	24.00	20.00	20.00	20.00	21.40	27.40

FOAM RESULTS (INCHES OF FOAM):

200 ppm Product - Initial:	5.12	5.37	2.12	5.75	3.75	2.25	4.75	0.00	4.62
5 Mins.	4.62	4.87	2.12	5.50	3.62	2.25	4.62	0.00	4.62
*Residual - Initial:	0.75	0.87	0.25	0.62	0.87	0.50	1.12	0.00	0.75
5 Mins.	0.50	0.62	0.12	0.37	0.62	0.50	1.00	0.00	0.75

* Ross-Miles equipment was thoroughly drained of the test solution and repeated with distilled water alone. The second foam height is indicative of solution clinging to the walls of the Ross-Miles and/or foaming capabilities of the dilute solutions of the surface active agent.

2. Antifoam

The candidate antifoam recommended is Dow Corning 536 fluid. As noted in the previous table, it defoams high-foam anionic surfactants when used at 10 ppm. Economics Laboratory, Inc. is considering a suitable dispensing mechanism similar to several of its commercial products.

3. Detergent Filming Buildup Study

The subject protocol is given in Appendix E. The purpose is to assess to what extent candidate formulations cause equipment filming. These formulations should be evaluated vs. a standard. The standard is recommended to be Prell.

This completes the Economics Laboratory, Inc. final report to NASA on NAS9-17428, EL 04-85-GC1.

October 29, 1985

TABLE # 1 (Revised)
FOAM TEST RESULTS

<u>ITEM</u>	<u>NASA RESULT</u>		<u>ROSS MILES RESULT</u>		
	<u>Conc. of active* and Result</u>		<u>Conc. of active and Result</u>		
	<u>Low</u>	<u>High</u>	<u>Initial**</u>	<u>5 minutes</u>	
Surgi Bac - 0.19% solution	215 fail	430 fail	190	4.25	4.12
5.00% solution			9500	6.25	6.00
Surgi Bac with Calcium	215 pass	430 pass	190	0.50	0.25
Mironol JEM	215 pass	430 pass	210	0.75	0.25
Ammonium Lauryl Sarcosinate (30%)					
0.19% solution	215 pass	430 pass	300	1.50	.50
5.00% solution			15,000	7.75	6.50
Sodium N Coconut Acid	215 fail	430 fail	240	4.87	4.75
N-methyl tourate - 24%					
(Igepan TC42)					
NASA non-foaming soap			150	0.75	0.25
Showermate			≈ 200***	3.75	3.50
Ivory	200 fail		≈ 200	1.12	0.87
Mink Difference			≈ 200	1.75	1.75
Clairoil			≈ 200	3.50	3.25
Jhirmack			≈ 200	3.87	3.75
Finesse			≈ 200	5.00	4.75
Silkience			≈ 200	5.25	5.12

continued on Page 2

August, 1985

TABLE # 1 (Revised)

FOAM TEST RESULTS

ITEM	NASA RESULT		ROSS MILES RESULT		
	Conc. of active* and Result		Conc. of active and Result		
	Low	High	Initial**	5 minutes	
Lonza 12C (32%) Cocobetaine			320	4.25	4.00
Ninox L (30%) Lauryl dimethyl amine oxide			300	5.62	5.37
Steol CS 460 (60%) Alkylether sulfate sodium salt			600	5.62	5.50
HF066 (100%)			1000	2.37	2.25
Hamposyl C (100%) Cocoyl sarcosine			1000	0.75	0.75
Ammonium Lauryl Sulfate 28% (Sipon L-22)		Fail	280	2.50	2.25
Magnesium Lauryl Sulfate 27% (Sipon LM)		Fail	270	5.62	5.50
Alpha Olefin Sulfsinate 40% (Witconate AOS)		Fail	400	5.50	5.50
* Concentration expressed in ppm ** Height in inches *** Estimated concentration if shampoos are 20% active					
0.1% Concentration, except as noted Distilled water 25°C (room temperature)					
Cocoamphocarboxyglycinate 50% (Miranol C2M conc.)		Fail	500	5.62	5.25
Ammonium Lauryl Ether Sulfate 60% (Steol CA 460)			600	5.75	5.62

Prepared by:
Steve Lentsch

TABLE #2

INGREDIENTS	pH	Ivory "candle"	Finesse	Silkiness	Clairol Condition	Mink Difference	Whitmack	Softsoap Liq. soap	Liq. Shower Mate
Water		1							
Ammonium Lauryl Sulfate		2	1	1	1	1	1	1	1
Palmitic Acid		3	2			3			
Cocamide MEA		4				13			
Glycol Distearate		5						13	
Citric Acid		6	12	6	12	10	5		
Ammonium Chloride		7				6		7	
Fragrance		8	10	8	10	15	15	16	10
EDTA		9	11	10	7				14
Sodium Hydroxide		10							
Methylchloroisothiazolinone		11	13				13		
Methylisothiazolinone		12	14				14		
FD+C Yellow #5		13			15				
FD+C Red #4		14							
FD+C Blue #1		15	16				16		18
Cocamidopropylhydroxysulfate									
Glycerin			3					8	
Cocamide DEA			4						
PPG-30 Cetyl Ether			5						
Polysorbate-20			6						
Dimethicone Copolyol			7						
Hydroxypropylmethylcellulose			8						
D&C Red #33			9	9					
TEA-Lauryl Sulfate									
Lauramide DEA				2		4		4	3
Dihydroxyethyl Tallow Glycinate				3	3				5
Sodium Chloride				4		14		6	8
Boric Acid				5		5		14	15
Methyl Paraben				7	11	11	11		
D&C Yellow #10				11					
D&C Red #19				12					
Sodium Lauryl Sulfate				13	2				
Hydrolyzed Keratin					4				
Glycol Stearate					5		10	3	12
Imidazolidinyl Urea					6				
Lauryl Alcohol					8				
Hydrolyzed Animal Protein					9		12	15	16
Propyl Paraben					13				
Phenoxyethanol					14				
Other					16				
Ammonium Laureth Sulfate						2	2		
Ceteth-16						7			
Laneth-16						8			
Oleth-16						9			
Mink Oil						12			
Sterath-16						16			
Cocamidocarbonylglycinate									
Sodium PCA							3		
Hydrolyzed Yeast							4		
Silk Amino Acids							6		
Silk Powder							7		
Guar Hydroxypropyltrimonium Chloride							8		
D&C Red 28							9		
Sodium C14-16 Olefin Sulfonate							17		
Cocamidopropyl Betaine								2	2
Quat-33								5	7
Ethyl Hexanediol								9	
Quat-41								10	
DMDM Hydantion								11	
DEA Lauryl Sulfate								12	
Disodium Monococamide Miprasulfosuccinate								17	13
TEA-Oleate								11	4
Octyl Hydroxystearate								6	9
Oleth 20								10	10
Benzophenone								11	11
Table #2								19	19
pH	4.9		5.4	6.6	6.4	5.6	5.0	7.7	7.0

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APPENDIX A
DATABASE REFERENCES

NAS 9-17428 - EL 04-85-GC1

A Study To Define A Set of Requirements
For Cleansing Agents For Use in the Space Station
Whole Body Shower

October 29, 1985

TASK 1

Literature Search on Soaps and Surfactants included over 12 data banks including Chem. Abst., Medline, Excerpta Medicur, NTIS, Dissertation Abst., Scisearch, Sov. Sci. and Tech., Conf. Papers, etc. The articles had some overlaps, that is, papers primarily directed toward formulations may have included toxicological information and vice versa. For the purposes of this study, these articles were divided into the following categories which will serve to focus our attention on certain important criteria. The following outline represents our focus and summary on the list of articles retrieved in this search.

1. Skin:

a. Irritation

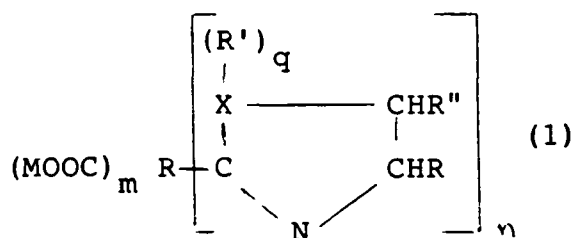
1. A Comparison of The Skin Irritation Produced by Cosmetic Ingredients and Formulations in the Rabbit, Guinea Pig, and Beagle Dog to that observed in the Human.
F. S. Kilmer MacMillan, et al.
Dermatotoxicol. - 1975
Selective and carefully controlled animal studies provide a useful function in the evaluation of the safety of topical cosmetic formulations. This is particularly true when the test procedure was adapted in accordance with the type of formulation under investigation. In the final analysis, however, there can be no substitute for the skin of man in testing topical preparations for irritancy under both exaggerated and conditions approaching normal usage.
2. Protective effect of collagen upon irritation response of detergents.
P. Morganti, et al.
International Journal of Cosmetic Science
5,7-14(1983)
Collagen probably forms a film around the individual detergent micelles and thus moderates the action of soap and synthetic detergent bar. This protective effect can also be explained by a mechanism involving absorption of the collagen on the outer surface of the 'stratum corneum'.
3. A Statistical Approach to the Evaluation of Cutaneous Responses to Irritants.
W. M. Wooding, B.Ch.E., et al.
J. Soc. Cosmetic Chemists, 18,809-820 (Dec.9, 1967)
Sodium lauryl sulfate, a typical irritant of general

interest was used. Two experiments are described in which several factors thought to affect irritation results were tested these included irritant concentration, certain time factors, and types of patch used. One of the significant effects of considerable interest was the finding that the degree of observable irritation was a function of the interval between removal of a patch and the time the site was scored.

4. A comparison of predictive irritation tests with surfactants on human and animal skin.
V. K. H. Brown
J. Soc. Cosmet. Chem. 22 411-420 (1971)
Nine DETERGENT base materials have been examined in a series of in vivo and in vitro TESTS involving the use of HUMAN SKIN and various ANIMAL SKINS. Lack of agreement between the results from different tests was apparent and a cautious approach to predictive SKIN-IRRITANCY testing with detergents is advocated.
5. Factors which determine the skin irritation potential of soaps and detergents.
Colin Prottey, et al.
J. Soc. Cosmet. Chem. 26 29-46 (1975)
Effects of pure surfactants upon the STRATUM CORNEUM have been studied by means of KERATIN denaturation and the extraction of PROTEINS and AMINO ACIDS. It was found that strongly ANIONIC SURFACTANTS, such as sodium LAURYL SULPHATE, sodium LAURYL ETHER SULPHATE and sodium LAUROYL ISETHIONATE (Igepon A) had considerable activity, by virtue of their polar head groups, whereas sodium laurate and non-ionic ethoxylates had minimal effect upon the stratum corneum. The effect of lipophilic chain length of the surfactants was important in their overall activity, in particular, the lauryl moiety. PERCUTANEOUS ABSORPTION OF RADIOACTIVELY-LABELLED surfactants by guinea-pigs in vivo has been studied. The effect of pure surfactants upon living cells was studied by means of measuring HISTAMINE release from rat peritoneal MAST CELLS in vitro.
6. Interspecies Comparisons of Skin Irritancy.
G. A. Nixon, et al.
Toxicology and Applied Pharmacology 31, 481-490 (1975)
In a series of patch testing experiments, 24 familiar household materials or industrial chemicals were applied to intact and abraded skin of rabbits, guinea pigs, and humans for four hours. A number of materials caused greatly different reactions from one species to another. Neither rabbit nor guinea pig skin should be relied upon exclusively to identify potentially hazardous irritants to human skin and

7. U.S. Patent 3,846,554 - November 5, 1974

Reduction of skin irritation caused by skin irritating detergent or detergent composition is achieved by incorporating in the irritating detergent or detergent composition an effective amount of a protective agent of the formula.



Edward A. Tavss, et al.

9. U.S. Patent 4,488,564 - December 18, 1984

Jean F. Grollier, et al.

10. U.S. Patent 3,538,009 - November 3, 1970

Ralph Kelly, et al.

The degree of skin irritation of detergent compositions is reduced by adding to the detergent composition small amounts of polymerized fatty acid or salt thereof, e.g. dimer acid.

11. U.S. Patent 4,137,191 - January 30, 1979
John W. Lohr
A low irritant surfactant composition particularly adapted for shampoos and other light duty cleansing applications, comprising substantially equimolar amounts of a betaine surfactant and an amine fatty alcohol sulfate or sulfonate in a high boiling water miscible, polar, organic liquid.
12. U.S. Patent 4,414,144 - November 8, 1983
Marvin Liebowitz, et al.
An aqueous skin cleaning composition containing hydroxypropylated guar gum, paraffin sulfonate, and C₈₋₁₆ alkyl sulfate, and a method of washing the skin therewith.
13. U.S. Patent 4,261,851 - April 14, 1981
Roland P. Duke
A detergent composition for skin cleansing or care of the hair, comprising at least two surfactants, one being of a particular nonionic type and another being of a different type such as an amphoteric/anionic surfactant. The non-ionic surfactant has a thickening effect and is typified by diacidic and triacidic acid reaction products of alkoxylated polyol fatty esters.
14. U.S. Patent Re. 28,913 - Reissued July 20, 1976
Ralph Kelly, et al.
The degree of skin irritation of detergent compositions is reduced by adding small amounts of a hydroxyl derivative of a polymerized fatty acid or a hydroxyl derivative of a hydrogenated (saturated) polymerized fatty acid, e.g. the hydroxy derivative of dimer acid.
15. Verbesserung der dermatologischen Eigenschaften von Tensiden
A. Domsch/G. Schuster
Arztliche Kosmetologie 13, 524-530 (1983)
Improvement in the dermatological properties of surfactants by protein hydrolyzate and protein-fatty acid condensates.
16. Toxicity of Handcleaners
W. G. van Kelel, et al.
Dermatologica 168:94-99 (1984)
The irritancy of commercially available liquid handcleaners was determined by means of soap chamber test (with Big Finn Chambers^(R)). Alkaline soaps were not extra irritating than other handcleaners. The cleaner with the highest irritancy score had a low pH. It was concluded that the pH was not a useful parameter to predict the irritancy of handcleaners.

October 24, 1985

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17. Determinacion del potencial de irritacion de productos tensioactivos en piel humana, metodos "in vitro"
F. Balaguer
Invest. Inf. Text. Tensioactivos - 1979, V. 19, #4
In vitro determination of the irritation potential of surface-active products on human skin. In Spanish.
The article not translated.
18. Les dimethicones copolyols, evaluation de leur pouvoir anti-irritant
Michael Starch, et al.
Parfums, cosmetiques, aromes n° 58 - aout-septembre 1984
Dimethicone Copolyols: Evaluation of their anti-irritant capabilities. In French. Not translated.
19. Effect on the skin of shampoos prepared from synthetic surface-active agents
H. M. Typahob, et al.
Vestnik Dermatologii Venerologii - 1973 V. 12
In Russian. Not translated.
20. Effect of Solid Detergent Washing on Values of Skin Electrical Impedance
L. Bernardi, et al.
Bolletino-Societa Italiana Biologia Sperimentale - 1982 - Vol. 58, #20
The results have shown that the cleaning has globally reduced the electrical skin impedance of the forehead, without influencing other parts examined (dorsal and palmar surfaces of the hand). The result has been attributed to the elimination of the hydrolipidic film of the surface and in particular that of the sebum of the forehead.
21. The Rabbit As A Model For Evaluating Skin Irritants: A Comparison of Results Obtained On Animals And Man Using Repeated Skin Exposures
F. N. Marzulli, et al.
Fd Cosmet. Toxicol. Vol. 13, pp. 533-540
A new animal test for evaluating the skin-irritant capacity of cosmetic and drug preparations and ingredients intended for repeated application is presented. Results on 60 test materials showed a significant correlation ($r = 0.30$; $P < 0.02$) between the cumulative irritation scores obtained on rabbits and those obtained on man. The usefulness and limitation of single-application (Draize type) and multiple-application tests for skin irritation are discussed.

22. The Influence of Concentration, Exposure Duration, and Patch Occlusivity Upon Rabbit Primary Dermal Irritation Indices
M. R. Gilman, et al.
Drug and Chemical Toxicology, 1(4), 391-400 (1978)
The Primary Rabbit Dermal Irritation Assay as described in the Federal Hazardous Substances Act (FHSA) is used by the Consumer Products Safety Commission (CPSC) to determine the labeling requirements of household products. Experimental findings show that form and concentration well as the length of contact with the skin and the degree of patch occlusivity are prime factors influencing the degree of skin change.
23. Republic of South Africa Patent 68/1096 - February 2, 1968
Ralph Kelly, et al.
See U.S. Patent No. Re. 28,913, Reissued July 20, 1976.
24. Czechoslovakian Patent 193,909 - January 1, 1982
Jan Novak, et al.
Washing and Rinsing Agent without harmful effect on the skin. In Czechoslovakian. Not translated.
25. French Patent 1.468.292 - December 26, 1966
M. Carl Martin Anshelm
Inhibition of Skin Irritation Due to Surface-Active Substances in Textiles.
26. Etude Du Picotement Par Contorsion Chez La Souris: Applications A L'Evaluation Du Potentiel Irritant Des Agents Tensio-Actifs Et Des Shampoings
"Evaluation of discomfort in the mouse by contorsions; testing the irritation potential of surfactants and shampoos. In French. Not translated.
27. "Test for skin damage caused by detergents."
Dr. Gy. Kiss
Dermatosen Beruf Umwelt - 1981, V. 29 #1
With the aid of an electric impedance test the author studied the effects of the washing ingredients on the skin. From his investigations he came to the conclusion that the different ingredients only cause slight irritation when in the same concentration as that found in water used for washing. Their effect is however cumulative and depending on patient's resistance capability, still may cause dermatitis.
28. Skin Tolerance Index of Newly Developed Syndets.
M. Puschmann/J. Meyer-Rohn
Arzlich Kosmetologic 13, 225-234 (1983)
Recently developed syndets were tested on their skin tolerance against traditional syndets based on sodium laurylsulfate. In contrast, with sodium laurylsulfates a significantly higher irritation potential was observed. The novel syndets were very well tolerated by the skin.

29. Action of Surfactants Upon the Skin

Kikuhiko Okamoto

Yukagaku - 1974, Vol. 23, #11

Desquamative Change of the Skin Surface, Irritation of the Skin and Inhibition of Invertase Activity by the Surfactants. In Japanese. Not translated.

b. Defatting

1. Effect of Polyoxyethylated Materials on the Interaction of Surfactants with Skin

J. A. Faucher, et al.

Jnl. American Oil Chemists Society - 1979, V. 56, #8

Permeability studies indicate that typical cationic and nonionic surfactants are weak penetrants, unlike anionic surfactants, as exemplified by sodium lauryl sulfate which readily penetrates and tends to destroy the integrity of stratum corneum membranes in a matter of hours. The addition of polyethylene glycols results in a considerable reduction in the last mentioned effects. By contrast, the electrophysiological measurements show that cationic surfactants can be extremely active: cetyltrimethyl ammonium bromide at a level of 0.5% destroys the potential across frog skin in minutes.

2. Study on Skin Roughness Caused by Surfactants:

1. A New Method in Vivo for Evaluation of Skin Roughness

G. Imokawa, et al.

Jnl. American Oil Chemists Society - 1975, V. 52 #12

A simple and accurate method for evaluating skin roughness caused by surfactants has been developed. Results indicated in general, that the surfactants having 12 carbons in their alkyl chain gave the skin more roughness than did those which had more or less than 12.

3. Prediction and measurement of surfactant action upon human skin under realistic conditions

C. Prottey, et al.

International Journal of Cosmetic Science 6, 263-273 (1984)

The lysosomal enzyme acid phosphatase has been characterized and quantified in tape-strip biopsies of human stratum corneum by means of a sensitive spectrofluorometric procedure. When the stratum corneum of panellists was exposed to dilute solutions of various surfactants under realistic exposure conditions, the changes observed in stratum corneum acid phosphatase specific activity have been found to correlate very closely with the visual, macroscopic changes such as dryness and flakiness, that are elicited in skin as a result of surfactants.

4. Softener Yields Model for Skin Structure
Richard Seltzer

C&EN - July 15, 1985

Below a certain level of water content, skin lipids form an agglomerate of solid crystals, giving a dry, coarse appearance and feel to the skin. On the other hand, when the water content is raised, the lipids form a liquid crystal, with a smooth structure. If humectants, such as glycerol, are used, they replace water in the skin structure, but they are easily washed away. Glyceridacid 100 interacts with and changes the structure of epidermal lipids. This enables retention of the liquid crystals and the glossy, smoother appearance at lower water content.

5. Cutaneous Effects of Household Synthetic Detergents and Soaps

R. R. Suskind, et al.

Archives of Dermatology (Amer. Med. Assn. Publ.)

Vol. 88, No. 2, August, 1963

From these observations it was concluded that in household usage soap or synthetic detergent immersion alone may not be the primary provoking stimulus in housewives' dermatitis. The role of other critical factors such as temperature and humidity are discussed.

6. Instrumental evaluation of the effects of cosmetic products on skin surfaces with particular reference to smoothness

J. K. Prall

J. Soc. Cosmet. Chem. 24 693-707 (1973) (Great Britain)

Some of the more important variables are discussed resulting from experience in measuring those PHYSICAL PROPERTIES which contribute to the overall TACTILE PERCEPTION OF SKIN SMOOTHNESS. This expresses smoothness in terms of surface topography, FRICTION and HARDNESS. The SENSITIVITY and potential usefulness of these techniques is illustrated by reference to some important product TREATMENTS which can affect the WATER CONTENT of the STRATUM CORNEUM.

7. U.S. Patent 3,906,106 - September 16, 1975
Jacobi, et al.

A composition containing one or more esters formed from an aliphatic, branch chain, fatty alcohol having at least 8 carbon atoms in the molecule and a hydroxy fatty acid is described. The composition can be applied directly to the skin or can be added to cosmetic or pharmaceutical products and provides an irritation reducing, refattening effect on the skin.

8. pHresh 3.5: A New Low pH Liquid Skin Cleanser
William V. R. Shellow, et al.
J. Int. Med. Res. (1981) 9, 297-299
pHresh 3.5, a new low pH liquid skin cleanser, was evaluated for safety and efficacy in four clinical studies. In 5- and 21-day predictive patch tests the cleanser was rated mild compared to four other widely used cleansers.
9. Effect of surfactants on skin surface film.
I. Defatting in relation to concentration and constitution.
G. Wuerbach, et al.
Dermatol. Monatsschr. 169 (1983) 243-247
After washing experiments on the human back using a special washing apparatus there were found differences in the defatting qualities of the investigated surfactants; with regard to chemical constitution the slightest defatting effect beside the carboxylic amide betaine was given by the investigated sulfosuccinate compared with the vigorous lipid emulsifying power of sodium dodecylsulphate.
10. Surface Activity and Cutaneous Effects of Monoalkyl Phosphate Surfactants
G. Imokawa, et al.
Jnl. American Oil Chemists' Society, Vol 55 - Nov. 1978
Monoalkyl phosphates of high purity were synthesized and were investigated for their surface-active properties and cutaneous effects. These surfactants possess adequate surface-active properties similar to those of common anionic surfactants and they exhibit considerable safety on the skin in comparison with typical anionic surfactants used commercially.
11. Diminishing The Skin - Drying Effect of Detergents
H. Tronnier, et al.
Soap, Perfumery Cosmetics, July, 1968
Studies on the removal and replacement of skin fats by the use of solutions containing surfactants, with and without the addition of lipids.
12. Effect of alkyl sulfates on skin
E. A. Hebneba, et al.
Neftepererabotka Neftekhimia (Moscow), 1972, #3
Did not translate.

13. Irritating action of surfactants on skin dependent on their molecular structure
E. A. Hebneba, et al.
Maslo-Zhirovaia Promyshlennost - 1972, V. 38, #5
Did not translate.
14. Effect on the skin of some synthetic detergents containing the disodium sulfosuccinic acid monoesters
B. B. Heanob
Vestnik Dermatologii Venerologii - 1973
Did not translate.
15. Common Sense Care for Aging Skin
John M. Knox, M.D.
Geriatrics/February 1975, 30, #2, 59
Avitaminoses are more common in the elderly than in any other age group, and physicians should be alert for cutaneous signs indicating a deficiency of one or more vitamins in these patients.
16. Performance of dialkyl suphate-lauric monoethanolamide-PVP/VA shampoo in the presence of superfatting materials
A. A. Kassem and S. A. Said, Ph.D.
Cosmetics and Perfumery, 88, 35, 1973
The effect of several superfatting materials, namely lauric acid hexyl ester, oleic acid decyl ester, oleyl cetyl alcohol, and 2-octyl dodecanol, on the performance of a shampoo containing 15% of sodium lauryl-myristyl alcohol ether sulphate, 1.5% of lauric monoethanolamide, and 4.0% of PVP/VA 73-copolymer was studied.
17. Czechoslovakian Patent 198368 - March 15, 1977
Jan Miars
Not translated.
18. Effect of alkyl sulfates on skin.
Neftepererabotka Neftekhimia (Moscow)
1972, #3
Did not translate.

c. Dermatitis/Allergy

1. A Chemical Measure of the Effect of Soaps and Detergents on the Skin
E. J. Van Scott, et al.
Journal of Investigative Dermatology, Vol. 21, pp. 199-203 (1953)
Various types of keratin (stratum corneum, nails, hair) were incubated in solutions of soaps and detergents. By This treatment the measurable amounts of sulfhydryl groups were increased over those of control solutions. These findings indicate a certain denaturing effect of these substances on the keratin molecule. The possible role of this effect in the production of dermatitis from these substances is discussed.
2. The interaction of detergents and the human skin
Professor Dr. Machiel K. Polano, et al.
J. Soc. Cosmetic Chemists 19 3-20 (1968) (Great Britain)
Detergents can irritate a normal skin. Suskind's results are only valid for the detergents which he used and for his experimental conditions; their application to all detergents under all conditions is not warranted. He studied the hands primarily. The skin of the arms proved to be more sensitive.
3. Skin Sensitization Potential of Alpha-Olefin Sulfonate (AOS) and a Prototype Dishwashing Detergent Containing AOS.
P. H. S. Bay, et al.
JAOCS, Vol. 62, No. 4 (April, 1985)
The degree of response appeared to be dose-related to the amount of alkyl gamma-unsaturated sultone (US) present in the material being tested.

4. Antimicrobials: Experimental contact sensitization in man
F. N. Marzulli, et al.
J. Soc. Cosmet. Chem. 24, 399-421 (1973) (Great Britain)
The data show that organic and inorganic mercurials, FORMALIN, bronopol, mafenide, captan and chloroacetamide have relatively stronger skin sensitization potential (5% sensitization index). Propylene glycol, triclocarban, chlorinated phenolics such as HEXACHLOROPHENE, chloroxyleneol and dichlorophene, and PARABENS and tribromsalicylanilide and possibly sorbic acid appear to be relatively lower grade SENSITIZERS (0-0.5%) sensitization index.)
5. Parallergerizing effect of various synthetic detergents on the skin.
B. B. Heahob
Vestn. Dermatol. Venerol. - 1975, V. 3
In Russian. Not translated.
6. OTC Drug Products for the Control of Dandruff, Seborrheic Dermatitis, and Psoriasis
Herman E. Jass
Cosmetics & Toiletries, Vol. 98, February, 1983
The major ingredients presently in use for the control of dandruff; pyrithione zinc, selenium sulfide, coal tar, sulfur, and salicylic acid, were all placed in Category I.
7. The Effect of Membrane Detergents and Retinoic Acid on Membrane Microviscosity
Robert G. Meeks, et al.
Federation Proceedings - 1979 - Vol. 38, #1645
The effect of several membrane detergents and retinoic acid on the microviscosity (η) of biological membranes including rat erythrocyte ghosts was studied. Rat erythrocyte membranes (REM) showed a linear dependence of η when presented as log vs. $1/T$ with a fusion activation energy (ΔE) of 8.2 kcal mole⁻¹.
8. Role of Sultone Contaminants in an Outbreak of Allergic Contact Dermatitis Caused by Alkyl Ethoxyfulphates: A Review
W. E. Lindup, et al.
Fd. Cosmet. Toxicol. Vol. 16, pp. 59-62 (1978) Great Britain
An outbreak of severe allergic contact dermatitis occurred in Norway in 1966 in women who had used a new dish-washing product containing an alkyl ethoxysulphate. Investigations revealed the presence of unsaturated sultone and chlorosultone contaminants. Their presence was attributed to abnormal manufacturing conditions. These sultones were shown to be poten

skin sensitizers and the allergic contact dermatitis was attributed to them.

9. Identification of Certain Sultones as the Sensitizers in an Alkyl Ethoxy Sulfate
D. S. Connor, et al.
Fette Seifen Anstrichmittel - 1975, V. 77, #1
Skin sensitizing agents that were present in a specific batch of alkyl ethoxy sulfate (AES) were identified as 1-dodecene-1,3-sultone and 1-tetradecene-1,3-sultone. Two other sensitizing agents that were present in the AES were tentatively identified as 2-chloro-1,3-dodecane-sultone and 2-chloro-1,3-tetradecane-sultone.

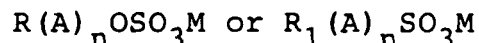
2. Eye:

. Irritation/Damage/Smarting

1. Evaluation of the Corneal Irritancy of Test Shampoos and Detergents in Various Animal Species
L. L. Gershbein, et al.
Fd. Cosmet. Toxicol., Vol. 15, pp. 131-134, 1977 (Great Britain)
Four commercial shampoos, two cationic detergents (2% Roccal and 2% Isothan Q-15, a nonionic agent (20% Neutronyx 600) and a 1:1 (v v) mixture of the last two products were instilled into the eyes of several animal species. To evaluate corneal change, the area intensity and vascularity of the opacity were rated and scored. In a few instances the eyes were rinsed with water after the test agent had been in contact with the cornea for a short period in these cases the initial contact of the agent with the cornea was shown to be critical. Corneal sensitivity was highest in the rabbit, hamster and mouse, intermediate in the rat and guinea pig and possibly lowest in the dog, cat, rhesus monkey and chicken.
2. Dose-Response Studies with Chemical Irritants in the Albino Rabbit Eye as a Basis for Selecting Optimum Testing Conditions for Predicting Hazard to the Human Eye
John F. Griffith, et al.
Toxicology and Applied Pharmacology 55, 501-513 (1980)
Twenty-one chemicals, solutions, and mixtures with different degrees of recognized irritant potential to the human eye were tested in albino rabbit eyes at dose volumes of 0.003, 0.01, 0.03, and 0.1 ml. Maximum irritation scores and median number of days for eyes to return to normal were compared with available data on human experience as a basis for selecting the

dose volume that would best predict human response. A dose volume of 0.01 ml most often gave results that were consistent with information on effects of human exposures. Corneal application of 0.01 ml of material is proposed as a more realistic test of eye hazard than is the Draize test.

3. U.S. Patent 4,412,944 - November 1, 1983
George W. Panzer, et al.
The composition contains an alkyl ether sulfate having the following structure formulae:



wherein R is an alkyl, alkylaryl, acyl or alkenyl group, most preferably 14 to 24, carbon atoms in the alkyl chain; R_1 is an acylamide group having most preferably 14 to 24, carbon atoms. A is an alkyl ether, the preferred group being ethoxy; n is preferably about 10 to about 20; and M is a cation such as an alkali metal, ammonium, or an alkanolamine. These compositions are particularly useful as cosmetic cleaning compositions, such as shampoos and bubble baths.

4. Testing Shampoos on rabbit eyes
H. Geleick, et al.
Seifen-Ole-Fette-Wachse-107.Jg.-Nr.15/1981
In German. Not translated.
5. An in vitro test for the assessment of eye irritancy in consumer products--preliminary findings
M. York, et al.
International Journal of Cosmetic Science 4, 223-234 (1982)
An in vitro procedure for preliminary screening of severe eye irritants is described. Rabbit eyes are removed immediately after death and are placed in temperature controlled chambers. The eyes are superfused with isotonic saline and, after a suitable equilibration period, are treated with test substances. Results of this in vitro tests show a reasonably good correlation with in vivo data for a series of chemicals reported in the literature to be severely, moderately, or non-irritant to eyes. The effects of shampoos in the vitro system are described, with preliminary results suggesting that the method can distinguish between normal 'adult' shampoos and 'baby' shampoos, which are known to differ in irritancy in vivo.

6. Testing Methods, and Species Specificity
W. Morton Grant,
Toxicology Of The Eye, Second Edition (1974)
In attempting to reduce the differences between rabbit and monkey eye responses to topical testing, Buehler and Newmann have shown that if in the rabbit the contact of the test substance is limited to the cornea by means of an applicator cup, the lesions are much more like those produced by an exposure of the whole external surface of the monkey eye, and therefore more like responses of the human eye.
7. Evaluating the potential eye irritancy of shampoos
Melissa Bell, et al.
International Journal of Cosmetic Science 1, 123-131 (1979)
Detergent concentration is the principal factor influencing findings in the rabbit eye and an active matter content of 2.5-3.0% (usually representing a 20% aqueous dilution of shampoo) gives the best discrimination between formulations whilst producing no signs of distress in the animals; for typical anionic shampoos, testing at this concentration is recommended without subsequent rinsing. For preliminary screening, an in vitro test using freshly-isolated buccal mucosa cells from human volunteers may be useful, irritancy being assessed by the proportion of cells showing loss of visible nuclei when examined by phase-contrast microscopy.
8. Methode d'evaluation du picotement oculaire de shampooings et de certains tensio-actifs chez la souris
K. G. Dossou, et al.
Labo-Pharma-Problemes et Techniques - No. 286, Vol. 27, April 1979
The authors propose a simple method for evaluating accidental eye irritation that might be caused by cosmetic or other products. Their work centers on finished products, shampoos, and raw materials, surface-active agents, requiring particular mildness or non-stinging properties, for example, baby shampoo which should neither sting nor cause tears. The method is an adaptation of the writhing test used on mice currently practiced in pharmacology to detect the degree of activity of analgesics.
9. Study on the ocular tolerance of surfactants used in shampoos
J. J. Serrano, et al.
Parfums, cosmetiques, aromes n° 13--janvier/fevrier 1977
In French. Not translated.

10. Rain Soaked Hair

Transactions St. John's Hospital Derm. Soc. (England) -
1974, Vol. 60, #1

All shampoos and hair products are fully tested during product development before marketing, for possible irritation in the case of accidents. However, when rinsings of human hair after usage of the hair cream were collected and tested in the rabbit eye corneal damage was produced after the lapse of a few hours. The next stage was to test individual ingredients of the hair cream. When this was done only the 13-mole ethoxylated oleyl alcohol gave any response. Longer chain molecules are more hydrophilic and maximal enzyme inhibition is found with 10-20 ethylene oxide units. It is likely that some physico-chemical and possibly other change takes place in the hair cream constituents after usage on the hair.

11. Shampoo Composition Mild To The Eyes

Japanese Patent No. 54-56614
In Japanese. Not translated.

12. Corneal Anesthesia Induced by Soaps and Surfactants,
Lack of Correlation in Rabbits and Humans

Laurence S. Harris, et al.

Ophthalmologica, Basel 170: 320-325 (1975)

Five commonly marketed bath and facial soaps and four commercially available hair shampoos were studied for their anesthetic effect on human and rabbit corneas. These compounds all produced anesthesia comparable to that induced by tetracaine hydrochloride 0.5% but last several hours longer in rabbits. None of the soaps or shampoos produced corneal anesthesia in humans. Studies of corneal anesthesia in rabbits may not be extrapolated to the human eye.

13. Eye Irritation Testing of Shampoos

William R. Markland

Cosmetics & Toiletries, Vol. 96, September 1981

The procedure calls for dilution of the test shampoo to a specific level of active concentration, and direct comparison with an established control shampoo. The investigators offer a convincing rationale for these modifications and make the point that rabbit eye testing of shampoos should be regarded, not as a facsimile representation of likely human effects, but as a means of comparing the relative eye irritancy of shampoo formulations.

3. Hair

a. Damage/Prevention

1. Whole Coal Tar Shampoo: A Therapeutic Hair Repair System
S. Olansky

Cutis, Volume 25, 99, January 1980

An alkaline whole coal tar shampoo has been clinically re-

evaluated for its therapeutic and cosmetic properties. Its efficacy, as anticipated, is confirmed in psoriasis, dandruff, seborrheic dermatitis, and pruritis. Scanning electron microscopy reveals the whole coal tar shampoo's ability to repair hair similar to protein cosmetic shampoos.

2. The Effect of a Shampoo to the Hair, Skin and Hair Follicle (Human and Animal)

Yasushi Watanabe

Yukagaku - 1972, V. 21, #12, 909

In Japanese. Not translated. Summary and Tables and Figures all in English. The shampoo showed no effect on the hair. No positive reactions were found in the human patch tests under 4 hrs application of the shampoo itself and 10 hrs application of 5% solution of the shampoo. As for the animal tests, little effects on the skin were observed at 10% level of treatment. Though, in case of shampoo itself, an irritative reaction was found on the epidermis of some kinds of animals, but no obvious change of hair follicles was observed.

b. Shampoo Testing

1. Rheological properties of soap foam: 1. apparatus for viscoelastic measurement on foam

H. Komatsu, et al.

J. Soc. Cosmet. Chem., 29, 237-246 (May 1978)

An apparatus was devised to measure the RHEOLOGICAL PROPERTIES of toilet SOAP FOAM. The principle of the measurement was based on the analysis of oscillation damped by foam. The MEASUREMENTS by this APPARATUS were conducted at about 2.5 Hz (cycles/sec) on the soap foams obtained from a 5% (wt/wt) toilet soap aqueous solution at 40°C. The diameter of each bubble remained about 100 μ while the specific volume varied widely with varying condition of the preparation. The storage shear modulus increased from 500 to 850 dynes/cm², as the specific volume of foam increased from 10 to 25 cm³/g. On the other hand, the dynamic viscosity was not much affected by the specific volume and was about 15 to 20 poise. The loss tangent, a parameter expressing energy dissipation, for the forms was calculated to be about 0.3.

2. A Shampoo Test for Measuring Foam in the Presence of Soil
Nelson F. Borys, et al.

JAACS, July 1981/599A (Paper No. 216)

A test method has been developed to allow evaluation of the foam stability of shampoo formulations with reliability and reproducibility. The procedure involves modification of a German Standard Test (DIN 53 902). This technique allows the utilization of sebum soil, resulting in a more practical and valid test.

3. Shampoo Lather A Reliable Test
J. Roger Hart
Cosmetics & Toiletries, Vol. 100, March 1985
The reliance on methods with little relevance to use conditions can be, and often are, very misleading. This is certainly the case with dilute, low mechanical action foam tests like the Ross-Miles and the familiar cyliner rotation and shake tests. With a more realistic lather test method, it has been shown that, alkanolamides, contrary to reputation, cause the lather to liquify. Triglycerides and water hardness improve the lather of alpha olefin sulfonate and sodium lauroyl sarcosinate. Simple betaines and amine oxides adversely affect the lather to a greater degree than the amidopropyl betaine and oxide.
4. Dermatologische Probleme im Zusammenhang mit der Applikation von Shampoos und Schaumbadern unter Berucksichtigung des Problems der Ruckfettung*)
M. Gloor
Parfumerie und Kosmetik, 54. Jahrgang, Nr. 8/73
Foam baths and shampoos mainly serve to clean skin or hair. In addition there is the desired or undesired secondary effect of the "degreasing of the skin". The relation of cleansing and degreasing action depends to a great extent on the kind of tensids or tensid mixtures used and the addition of so-called regreasing agents.
5. U.S. Patent 4,132,679 - January 2, 1979
Hisso Tsutsumi, et al.

U.S. Patent 4,132,679 - January 2, 1979
Hisso Tsutsumi, et al.
A liquid shampoo composition comprising an aqueous solution of (A) monoalkyl ester salt of phosphoric acid and (B) trialkylaminoacetobetaine, trialkylaminopropanesulfobetaine, or mixture thereof. The composition possesses high detergency, high foaming and low skin irritation properties.
6. U.S. Patent 4,177,171 - December 4, 1979
John M. Waltz
The composition has a high viscosity and good foaming properties. The composition is a mixture of (1) an amphoteric surfactant combined with an anionic surfactant and (2) a nonionic surfactant which is a 16-18 carbon atom fatty monoester of an aliphatic polyhydric alcohol reacted with 60 to 100 moles of ethylene oxide.

c. Dandruff

1. The effect of zinc pyrithione on human skin cells in vitro
Genji Imokawa, et al.
J. Soc. Cosmet. Chem., 34, 1-11 (Jan./Feb. 1983)
A highly active antidandruff agent, zinc pyrithione was investigated on human skin cells (JTC-17) to test the hypothesis that like selenium sulfide, it may also have an antimetabolic action on epidermis, acting on dandruff by reducing increased epidermal turnover. Analysis using synchronized cells revealed that zinc pyrithione can act on all periods of DNA synthesis to suppress it. These findings support the idea that zinc pyrithione may have an antidandruff effect by its antimetabolic action to the skin, rather than its antiyeast action.
2. Evaluation of efficacy of antidandruff agents
Eberhard Futterer
J. Soc. Cosmet. Chem., 32, 327-338 (November, 1981)
Data are given for shampoos and cream rinses containing the new antidandruff agent PIROCTONE OLAMINE in comparison to the corresponding nonmedicated formulations as well as to the same shampoo bases containing ZINC PYRITHIONE as a known efficacious antidandruff agent. Piroctone olamine has been demonstrated to be highly effective in the treatment of dandruff and more effective than zinc pyrithione at the same concentration ($p < 0.05$).
3. French Patent N° de publication 2.134.070
N° demeystrement national 70.08883 - March 12, 1970
Adolphe-Louis Bernard
Journal De Medecine De Lyon 1975, 56, pages 195-202
"Principles of formulation of cosmetic products against dandruff." In French. Not translated.
4. Annotations, The Lancet - July 1, 1967
Dandruff - 145 patients with dandruff were given one of three shampoos: (i) a standard shampoo base; (ii) a medicated shampoo containing tar; or (iii) the medicated shampoo with a 2% solution of the sodium salt of the sulpho-succinate of an undecylenic alkylolamide (SBU 185). After three months the shampoo containing SBU 185 showed a distinct advantage over the medicated shampoo alone.

5. The Medical Letter
Vol. 19, No. 15 (Issue 484), July 29, 1977
Treatment of Dandruff - Dandruff results from an increased rate of physiologic shedding of cornified or horny cells from the scalp. These cells separate as flakes of various sizes. A similar though less conspicuous process takes place continuously over the entire skin surface throughout life. The antidandruff agents considered most effective by Medical Letter consultants are those containing zinc pyrithione (Head & Shoulders; Zincon; Danex; Breck One; and others) or selenium sulfide (Selsun; Selsun Blue; Sul-Blue; and others. Some authors have suggested that these agents may act by reducing epidermal cell turnover (AM Kligman et al, J. Soc. Cosmet. Chem., 27:111, 1976).
6. Therapeutic Aspects of the Seborrhoea Oleosa and Pityriasis Simplex Capillitii
Max Gloor
Der Hautarzt 30, 236-241 (1979)
In German. Not translated. The treatment of seborrhoea oleosa capillitii should aim at inhibiting depletion of the sebaceous glands, lipid synthesis in the sebaceous gland and microbial lipolysis of the triglycerides in the scalp and hair lipids. In the treatment of pityriasis simplex capillitii (dandruff) one aims at achieving inhibition of mitosis in the epidermis and, if possible, an additional "keratolytic" effect.
7. Shorter Methods for Evaluating Antidandruff Agents
James J. Leyden, et al.
J. Soc. Cosmet. Chem., 26, 573-580 (December 1975)
Two schedules are described in which the efficacy of ANTIDANDRUFF AGENTS can be assessed in panels of 10 subjects. The first employs shampooing twice weekly for 3 weeks with clinical grading and CORNEOCYTE COUNTS (quantification of desquamating cells) once weekly and after a one-week follow-up. In the second, the test agent is applied once daily for 5 weekdays for 2 weeks. Corneocyte counts and CLINICAL GRADING are done 4, 8, and 12 days after the last exposure.
8. A Contribution to a New Test Method for Dandruff-Inhibiting and "Keratolytic" Action of Drugs
M. Gloor and H. Kohler
European Journal of Clinical Pharmacology 11, 377-380 (1977)
Free cholesterol in lipids from the scalp and hair is predominantly a constituent of epidermal lipids. Therefore, a reduction in cholesterol content induced by a drug indicates a reduction in cell turnover in the epidermis.

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9. An Evaluation of O-T-C Dandruff and Seborrhea Products
Kenneth W. Chesterman
Journal of the American Pharmaceutical Association
Nov. 1972, Vol. 12, #11
The sloughing of dry, dead keratin cells in abnormal amounts is sometimes referred to as seborrhea capitis sicca. The products available for treating seborrhea capitis fall into basically three therapeutic classifications--wetting agents, antiseptics and keratolytics. The keratolytic which shows the best results in controlled studies is selenium sulfide.
10. Do Shampoos Affect Dandruff?
Suzanne Alexander, M.B., B.S.
British Journal of Dermatology, Feb. 1967, Vol. 79, #2
The treatment of dandruff usually consists of advice to use shampoos, which nowadays contain a soapless cleanser, often with the addition of tar. Hair lotions containing spirit with or without tar are also frequently prescribed. Preparations containing selenium sulphide are effective, but as alopecia has been attributed to their use, and since they are poisons, many dermatologists prefer other preparations.
11. Role of Microorganisms in Dandruff
James J. Leyden, et al.
Arch Dermatol--Vol 112, March 1976
The studies demonstrate that the increased number of scalp microorganisms found in dandruff occurs as a secondary event to increased nutrients and that scalp organisms play no primary role in the pathogenesis of dandruff.
12. The Dandruff Story
Raymond Oliver, M.D.
The Central African Journal of Medicine
Vol. 28, No. 1, January, 1982
The author regards dandruff as a natural phenomenon. Shampooing often and regularly appears to be the best treatment to control dandruff.
13. A Comparison of Miconazole Nitrate and Selenium Disulfide as Anti-dandruff agents
Rekha A. Sheth, M.D., D.V.D.
Int. J. Dermatology, Vol. 22, March 1983
The anti-dandruff efficacy of two shampoos containing 2% miconazole nitrate and 2.5% selenium disulfide was compared in 15 subjects and eight subjects, respectively. The antifungal drug, miconazole nitrate, was found to possess anti-dandruff activity similar to selenium sulfide, a cytostatic compound.
14. The Aetiology of Dandruff and the Mode of Action of Therapeutic Agents
Sam Shuster
British Journal of Dermatology (1984) III, 235-242
The clinical and histopathological dissociation of

dandruff from early seborrheic eczema and psoriasis has not been made. *P. ovale* is the commonest associate of dandruff: remove it and the dandruff improves, recolonize and the dandruff recurs. How *P. ovale* induces dandruff is not clear; inflammation and desquamation with some increase in cell production is an end result. There is no evidence that anti-fungal agents act on dandruff other than by decreasing the anti-mitotic effect are unacceptable.

15. Study of the microbiology of the scalp in dandruff, seborrheic dermatitis and pityriasis amiantacea
C. Veller Fornasa, A. De Zio, E. Serrati, G. Bersani, A. Peserico
Giornale Italiano di Dermatologiae Venereologia 118, 227-279 (1983)
16. Dandruff and Seborrheic Dermatitis
Russell W. Eyre, M.D., et al.
NCMJ, December 1984
Everyone has dandruff to some degree. We all shed our skin every forty-five days. People with dandruff just shed their skin at a faster rate and in larger, visible, clumps of cells. When inflammation or redness occurs with dandruff the diagnosis is usually seborrheic dermatitis. The cause of seborrheic dermatitis is unknown. Stress, overwork, and infrequent shampooing may worsen the dermatitis.
17. Dandruff may be catching
Clinical and Experimental Dermatology (1984) 9, 212
C. M. E. Rowland Payne
This article differentiates "Dandruff" due to various species of *Trychophyton* from normal shedding of skin.
18. Chemotherapy of dandruff
Pharmaceutica ACTA Helvetiae, Vol. 47, 1972
It is apparent that the chemotherapy of dandruff may be approached in several different ways and that some widely-cherished ideas on the mode of action of some antidandruff agents may rest on dubious foundations. Whilst the eradication of *Pityrosporum* infection appears to be at present the appropriate target, it could be true that this infection is a consequence rather than a cause of dandruff.
17. Review Article - The Microbiology of dandruff
G. C. Priestly, et al.
British Journal of Dermatology (1976) 94, 469
Some baffling problems lie in the border country between dermatology and cosmetology. They seem too trivial to whet the appetite of most clinical dermatologists and research is mainly driven by pressures from the market-place. Dandruff is a good example. Modern investigative techniques have, so far,

only scratched the surface of dandruff, raising a cloud of conflicting ideas and reports.

d. Hair Conditioning

1. No attempt has been made to search this topic.
However, there is much information of this subject in reference books and trade journals.

4. Microflora of the skin

1. Duschbade und sein Einflub auf die aerobe Residentflora der menschlichen Haut
Albert A. Hartman
Arch Dermatol Res 267, 161-174 (1980)
The shower-bath supplement is added in a constant dosis directly to the shower-jet to obtain constant conditions of shower-bathing on the human skin. Different concentrations of the shower-bath supplement in neighboured areas of the skin can be avoided and this allows to make comparative investigations of the effect of shower-bath supplements to the normal human skin flora.
2. Quantitative Microbiology of the Scalp in Non-Dandruff, Dandruff, and Seborrheic Dermatitis
K. J. McGinley
J. Invest Dermatol - 1975 - English
3. Investigation of the Dynamics of the Automicroflora of Skin and Faces, and the Bacterial Contamination of the Underclothes of Mine Workers
Russian - 1984 Gigiena i Sanitariia (ISSN 0016-9900)
In Russian. Not translated.
4. Promising Methods for Early Laboratory Diagnosis of Infectious Diseases
Voenno-Meditsinskii Zhurnal
(ISSN 0026-9050) Dec. 1984 - Russian
5. Antibacterial properties of soap containing some fatty acid esters
N. K. Pandey, et al.
International Journal of Cosmetic Science 7, 9-14 (1985)
Natural compounds such as short to medium chain fatty acids and their derivatives, which are known to be germicidal, offer a viable alternative to chemical inhibitors. We report here the synthesis of sodium 2-lauroyloxy propionate and an in vivo method to test its substantivity on skin following its incorporation in soaps. Among several compounds tested, sodium 2-lauroyloxy propionate was found to be highly substantive in soap formulation.

5. Formulation Technology

1. Das Schaumverhalten von Tensiden -- bestimmt nach einer Schlagschaummethode
Ernst Ludwig Roehl
Parfumerie und Kosmetik, 58. Jahrgang, Nr. 9/77
This investigation includes fatty acid alkylolamides used as foam stabilizing agents and aminoxides, so-called superfatting agents and hairconditioning expedients as well as lipophilic substances (linalool and linalyl acetate) present in perfume compositions.
2. Shampoo Lather A Reliable Test
J. Roger Hart
Cosmetics & Toiletries, Vol. 100, March 1985
In order to accurately guide formulation, shampoo test methods must attempt to reasonably simulate actual use conditions and results. With a more realistic lather test method, we have shown: alkanolamides, contrary to reputation, cause the lather to liquify triglycerides and water hardness improve the lather of alpha olefin sulfonate and sodium lauroyl sarcosinate simple betaines and amine oxides adversely affect the lather to a greater degree than the amidopropyl betaine and oxide.
3. Foam Formation and Foam Stability
R. Matalon
Journal of the Society of Cosmetic Chemists, Vol. III, pp. 216-225 (Nov. 1952)
The wire frame technique adapted for study has been described in detail. Various factors controlling foam formation and foam stability, i.e., the rate of adsorption in the surface layer and the rate of desorption on compression of the lamina, have been followed, using the traction and retraction curves. It is concluded that foaming agents tend to stabilise the lamina during the retraction process.
4. Canadian Patent 1028957 - 780404
Leonard Mackles
A self-foaming essentially anhydrous aerosol spray shampoo composition comprising an anionic surfactant distributed in an aerosol propellant being soluble in propellant and being capable of forming substantial amounts of foam when applied to hair which is wet with water.

5. Canadian Patent 1029306 - 780411

Leonard Mackles

A self-foaming essentially non-aqueous shampoo gel composition comprising a solvent, at least one anionic surfactant and a gelling agent; solvent being non-volatile at room temperature but volatile at elevated temperatures of about 75°F, solvent being soluble in surfactant and being capable of being foamed by solvent; gelling agent being soluble in the surfactant but insoluble in solvent.

U.S. Patent 3,950,417 - April 13, 1976

Robert J. Verdicchio, et al.

High lathering detergent compositions having excellent foam stability and low ocular irritation comprise a member selected from the group consisting of surfactant alkylbetaines, alkylamidobetaines, alkylsulfobetaines, and alkylamidosulfobetaines; and anionic surfactant; and a water-soluble, polyoxyethylene derivative of a hydrophobic base as the nonionic surfactant in a weight ratio of about 1:1:3, respectively.

6. Formulating with Amine Oxides

Morris Weinstein, et al.

Household & Personal Products Industry, January 1979

Amine oxides have a flexibility which is offered by very few surfactants in today's market. This group of compounds is finding increasing application in both the cosmetic and household product area. Reasons for the increased usage are varied. The classical alkanol-amine foam boosters have had a recent history of price instability. Another reason for their popularity is their utility in "acid balanced" formulas due to their unique conditioning action. Very few surfactants being offered in today's market have the flexibility of amine oxides.

7. Ways to regulate the viscosity of cosmetic preparations

Alwin K. Reng, et al.

Cosmetics & Toiletries, Vol. 94, June 1979

Sodium chloride, ammonium chloride, sodium sulphate, etc., are used almost exclusively for viscosity regulation in cosmetics; they will specifically thicken only alkyl ether sulphate solutions. The aminoxides, the alkanolamides, and the betaines, fatty alcohol polyglycol ethers and esters are also frequently employed. Cellulose ethers are very suitable for the manufacture of highly viscous shampoos, shower preparations.

8. Foam Stability of Hand Dishwashing Detergents

Detergents and Cleaning Compounds Test Methods

Compendium - 1981 Addendum

Chemical Specialties Manufacturers Association, Inc., 1981

This method for measuring the foam stability of hand dishwashing detergents represents the revision of three methods first approved by CSMA in 1958. A task group was formed in December, 1975 to update the 1958 methods. This revision was approved by the Scientific Committee in December 1979.

9. Viscosity Considerations in Using Anionics in Shampoo Formulas
Ken Klein
D&CI/October, 1982
This study focuses on the following areas:
Cation type--sodium ammonium of triethanolamine
Ethoxylation--0,1,2,3 moles of ethylene oxide (not done for the triethanolamine)
Chloride type--sodium or ammonium
Alkanolamide--presence or absence of lauric diethanolamide
10. U.S. Patent 3,949,137 - April 6, 1976
Akrongold, et al.
A gel-impregnated sponge having at least two layers of which at least one layer is impregnated with a hardened gel material and at least one layer is unimpregnated sponge material, the impregnated layer having a fibrous or fur-like coating on its outer surface areas.
11. U.S. Patent 3,912,666 - October 14, 1975
Joseph George Spitzer, et al.
These structures are particularly suitable for use as applicator pads having a porous surface with a high proportion of open area, with a material such as a cosmetic, pharmaceutical, detergent, antimicrobial agent or abrasive which is contained in the pores thereof, and which can be removed.
12. U.S. Patent 3,557,006 - January 19, 1971
Peter J. Ferrara
A solid soap produced in the form of bars is disclosed, having a pH which ranges from slightly acidic to neutral. The bar of soap comprises two separate soap entities of different properties physically combined to form a unitary structure, the properties of which result from the interaction of the two soap entities in actual use.
13. Europeisches Patentamt 0 075 906 - 25.09.82
Winfried Ehrl, et al.
Hair and Body Cleaning Agent Containing Alkyl Sulfobetaine
In German. Not translated.
14. Formulating Mild Shampoos with Sulfosuccinate Surfactants
Tom Schoenberg
Drug & Cosmetic Industry/November 1983
Mildness and performance properties required for these mild shampoos can be easily achieved with blends of sodium laureth-3 sulfate, sulfosuccinates and a foam booster. These combinations provide equivalent, or even superior performance, as the more expensive glycinate and sarcosinate surfactants.
15. French Patent 2 421 605 - 3 avril 1978
Robert Raymond Albert Georges, et al.
Not translated.

16. U.S. Patent 4,439,355 - March 27, 1984
Divaker B. Kenkare
This invention relates to such products intended for conventional toilet soap uses, either as hand "soaps" or bath or shower soaps", which are elastic in nature, which include either anionic detergent(s) or mixtures of such detergent(s) and amphoteric synthetic organic detergent(s), gelatin and lower alkylene glycol or polyhydric alcohol, and which are essentially free of water.
17. Enzyme-Containing Toothpastes
Philip Alexander
Manufacturing Chemist & Aerosol News, December 1973
18. Shampoos using alkanolamines
A. D. McMahan
American Perfumer and Cosmetics, Vol. 84, April, 1969, pp. 55, 56, 58
The effect of alkanolamine salts on viscosity is inversely proportional to the degree of substitution of ammonia. That is, triethanolamine sulphate would not be used in a high viscosity formulation, whereas monoethanolamine hydrochloride would. Triethanolamine lauryl sulphate has very good storage properties and remains clear at temperatures below 0°C.
19. U.K. Patent Specification 1 518 807 - July 26, 1978
Vincent Paul Heuring
The present invention is based in part upon the discovery that the mildness properties of a liquid detergent composition can be enhanced by the use of an alkyl ether sulfate derived from an ethoxylated alcohol which has been subjected to stripping to remove unethoxylated and monoethoxylated material.
20. U.S. Patent 3,639,468 - February 1, 1972
Noburo Hayashi, et al.
This invention related to a process for preparing novel amphoteric surface active agents which can reduce the irritation to human skin and increase the detergency of anionic surface active agents when they are incorporated in a washing agent composition including a process for preparing N-alkyl N-hydroxyethyl- β -aminoethoxyacetic acid or N-alkyl N,N-bis (ethoxyacetic acid).
21. French Patent No. 1.526.808 - 22 avril 1968
Not translated. Non-foaming Shampoos Containing Non-ionic Surfactants

22. The Practical Evaluation of Shampoos

Marshall Sorkin, M.S., et al.

J. Soc. Cosmetic Chemists, 17, 539-551 (1966)

Appearance, performance during use, and effect on hair after use are the three major criteria by which shampoos should be evaluated. Within these three broad categories, 25 separate characteristics are enumerated. The importance of each of these and laboratory and beauty salon test procedures for evaluating shampoos are discussed.

6. Toxicity

1. Detergent Toxicity Survey

Van M. Seabaugh, et al.

AJPH, April, 1977, Vol. 67, No. 4, pp. 367-369

Applicable to household detergents, not to personal care products.

2. Safety Testing of Alkyl Polyethoxylate Nonionic Surfactants. I. Acute Effects

G. M. Benke, et al.

Fd. Cosmet. Toxicol., Vol. 15, pp. 309-318, Pergamon Press, 1977, U.K.

The acute dermal toxicity of these materials was low in rabbits and guinea-pigs but moderate skin irritation was produced under occluded patches after 24 hr (concentrations up to 10%). Patch tests on human skin produced only minor irritation after 4 hr at concentrations of 25 or 100%. Young guinea-pigs immersed to chest level for 4 hr in 25% alkylpolyethoxylates (AE_x) developed only slight irritation. AE_x surfactants and formulations were severely irritating to the rabbit eye but had a much less severe and more transient effect on the monkey eye. Rat studies indicated a low inhalation toxicity.

3. Safety Evaluation of Enzyme Detergents. Oral and Cutaneous Toxicity, Irritancy and Skin Sensitization Studies

J. F. Griffith, et al.

Fd Cosmet. Toxicol. Vol 7, pp. 581-593, Pergamon Press, 1969, U.K.

Laboratory tests on more than 700 human subjects of a variety of enzyme-containing detergents showed no adverse effect on mildness from the enzyme ingredient except under conditions of high concentrations, occlusion of the skin and prolonged contact. Clinical mildness tests on 5943 housewives, diaper rash studies on 360 infants, and repeated insult patch tests of 1478 men and women revealed no untoward effect from products containing the enzyme ingredients.

4. Uber die Abhangigkeit dermatologischer Eigenschaften waschaktiver Tenside von deren Kettenlange

Hagen Tronnier

Perfumerie and Kosmetic, 58. Jahrgang, Nr. 3/77

One of the factors responsible of this particularly bad skin compatibility of C₁₂ compounds certainly is the albumen injurious effect characteristic of these compounds. This effect causes the increased penetration of the compounds into the skin as well as

the higher toxicity within the skin.

5. Safety Testing of Alkyl Polyethoxylate Nonionic Surfactants. II. Subchronic Studies
N. M. Brown, et al.
Fd Cosmet. Toxicol. Vol. 15, pp. 319-324, Pergamon Press, 1977
The alkyl polyethoxylates were evaluated for subchronic oral toxicity (using rats) and percutaneous toxicity (using rabbits), and for human contact sensitization and skin mildness. Tests using over 500 human volunteers produced no evidence suggestive of sensitization to formulations containing 33% alkyl polyethoxylates. Usage tests of these polyethoxylate detergents in which the condition of the skin was monitored by dermatologists demonstrated that these products are comparable in mildness with other detergent products having years of safe marketing experience.
6. Effects of pyrithiones and surfactants on zinc and enzyme levels in rabbits
Robert C. Spiker, Jr., et al.
Am. Ind. Hyg. Assoc. J. (41), April, 1980
The effects of zinc pyrithione (ZnPT) and sodium pyrithione (NaPT) upon whole blood and plasma zinc and SAP levels of rabbits were monitored in this study. Both compounds are used as antimicrobial agents in various industrial applications and ZnPT is used in shampoo formulations as an antidandruff ingredient. These substances can be toxic to animals under certain exaggerated, non-use conditions however, the low skin permeability of ZnPT, in particular has rendered it quite safe for normal use in shampoos.
7. Miscellaneous
 - a. Antifoam
 1. Antifoams
R. D. Kulkarni, et al.
J. Soc. Cosmet. Chem., 30, 105-125
(March/April 1979)
Emphasis is given to silicone-based compositions whose introduction in this field some three decades ago led to major changes in antifoaming technology. Fundamental mechanisms involved in the antifoaming process are outlined and a description is given of some of the mechanisms of foam stabilization. Lastly, a new, experimental antifoam, of "transient character," is described and its possible applications are outlined. Its activity in aqueous foaming systems lasts for a limited period, thereafter the full foaming power of the solution is restored.
 - b. Evaluation/Testing
 1. Factor analysis in the evaluation of cosmetic products
Eric Baines
J. Soc. Cosmet. Chem. 29 369-384 (1978)
In the evaluation of most cosmetic products many attributes

must be investigated. These attributes are not necessarily independent and product performance can be described more simply in terms of a small number of underlying factors which adequately account for all the measured attributes. Factor analysis provides a mathematical method by which these factors can be identified and their contributions towards each of the attributes calculated.

2. Standard Test Method for Foam in Aqueous Media
(Blender Test)
Annual Book of ASTM Standards - Part 25
American Society for Testing and Materials, 1982
The increase in volume is determined by the increase in total height of test fluid including foam after blending for 30 s using a commercial-type blender with glass jar (see Note 2) at $25 \pm 1^{\circ}\text{C}$ ($77 \pm 1.8^{\circ}\text{F}$) agitating between 4000 and 13 000 rpm. The preferred range would be 8000 ± 1000 rpm.
3. Standard Test Method for Foaming Properties of Surface-Active Agents
Annual Book of ASTM Standards - Volume 15.04
American Society for Testing and Materials, 1983
This method covers the determination of the foaming properties of surface-active agents, as defined in ASTM Definitions D 459, Terms Relating to Soaps and Other Detergents.² The method is applicable under limited and controlled conditions, but does not necessarily yield information correlating with specific end uses. This is an adaptation of the Ross-Miles foam test.
4. Rapid Liquid Chromatography of Bacteriostats
Thomas Wolf, et al.
J. Soc. Cosmet. Chem., 24, 363-370 (May 23, 1973)
5. The Evaluation Of A Shampoo
Wm. W. Myddleton, D.Sc., F.R.I.C.
Journal of Society of Cosmetic Chemists - 1953
However important the practical shampoo test in the saloon may be, it is quite clear that a test on a single head can be misleading because different heads are not shampooed with equal facility. On the other hand, a single foaminess test carried out in the apparatus described will indicate a good shampoo.
6. A Quantitative Method for the Evaluation and Study of Shampoos
G. Barnett and D. H. Powers
Jnl. Society Cosmetic Chemists - 1951, Vol 2
The technique involves the use of wool yarn in the grease with known wool-fat content. An accurately weighed sample is gently scoured in a definite concentration of shampoo or detergent in a known volume of water for an exact time under standard conditions.

c. Packaging

1. U.S. Patent 3,912,666 - October 14, 1975
Joseph George Spitzer, et al.
The emulsified propellant compositions are stored in closed containers capable of withstanding an internal pressure sufficient to keep the propellant in the liquid phase at atmospheric temperature, and when the composition is withdrawn from the container to atmospheric pressure, the propellant volatilizes rapidly, and the foamed structure is formed within a few seconds.
2. U.K. Patent Specification 1 263 739 - 16 Feb. 1972
Dart Industries Inc.
This invention relates to packages filled with two compositions maintained isolated from each other within a container, such packages adapted for the mixing of the isolated compositions and dispensing of the resulting mixture from the container. Such packages are particularly useful in dispensing of compositions in aerosol form for shaving and other purposes and may in accordance with the invention be dispensed at ambient temperatures or in a warmed state.

d. Fresheners

1. U.S. Patent 4,434,086 - Feb. 28, 1984
Ira D. Hill, et al.
Described is a process for imparting an "air dried cloth" aroma to cloth, synthetic or natural, previously dried using a clothes drier, comprising the step of contacting the cloth prior to drying with an aroma augmenting or enhancing quantity of n-hexanal, n-heptanal, n-octanal, n-nonanal, n-decanal, n-undecanal, n-dodecanal, n-tridecanal, n-tetradecanal, n-pentadecanal.
2. The Solubilisation of Perfumery Materials by Surface Active Agents
Maurice Bell
Perfuming Household Products
The concept of HLB has been found useful in predicting the probable solubilising properties of surfactants. The optimum solubilising range lies between HLB values of 13.0 to 17.0. Mixtures of non-ionic surfactants blended to give an overall HLB value of 13 to 15 were to be preferred over single non-ionic entities. This article also contains a bibliography of recent patents relative to the above subject.

APPENDIX B
DERMAL SENSITIZATION STUDY

NAS 9-17428 - EL 04-85-GC1

A Study To Define A Set of Requirements
For Cleansing Agents For Use In The Space Station
Whole Body Shower

October 29, 1985

Economics Laboratory, Inc.
Appendix B
NAS9-17428 - EL 04-85-GC1

FDRL Protocol No. 210
9/85
Page 1 of 6

Study Title: Dermal Sensitization Study: Buehler Test

Testing Facility: Food and Drug Research Laboratories, Inc.
Waverly, New York 14892

Sponsor and Address:

Sponsor's Representative:

FDRL Study No:

Test Article

Sponsor ID:

FDRL ID:

Vehicle:

Positive Control: Dinitrochlorobenzene (Optional)

Schedule

Proposed Starting Date:

Proposed Completion Date:

Proposed Final Report Date:

Approval of Protocol

Study Director: _____ Date: _____

Sponsor: _____ Date: _____

A. Purpose - To evaluate the contact sensitization potential of the test article following repetitive dermal applications.

B. Choice of Test System and Route of Administration of Test

Material - Guinea pigs have been found to be the most suitable model for detection of weak allergens (Magnusson and Kligman, 1970). The Buehler test has been shown to be sensitive enough to detect moderate to strong sensitizers (Buehler and Griffith, 1975). The dermal route of administration corresponds to a likely route of human exposure.

C. Test Article - At least 100 ml (100 g) of the test article from the same batch or lot should be provided to complete the study. The Sponsor is responsible for maintaining records of the test article purity, source and other data required by 21 CFR Part 58.105. Storage conditions and safety precautions will be provided by the Sponsor.

D. Animals and Animal Husbandry - All housing and care shall conform to the standards established in "Guide for the Care and Use of Laboratory Animals" DHEW Publication No. (NIH) 85-23.

1. Species/Strain: Hartley-derived albino guinea pigs.

2. Source: Charles River Breeding Laboratories, Inc.

3. Age/Weight at Initiation: 4-12 weeks/approximately 300-500 grams.

4. Number/Sex: 10 females for the test groups and 6 females for each control group for the induction and challenge phase; 3 additional animals will be obtained for each test group and will serve as naive controls at the challenge. Additional animals will be obtained for the dose-range studies.

5. Identification: Ear notching, cage tag. The project number plus the individual animal number will comprise a unique identification number for each animal.

6. Housing: Individually housed in wire mesh bottom cages.

7. Food: NIH Animal Feed A, (Zeigler Brothers, Inc., Gardners, PA), ad libitum. No known contaminants are expected to be present in the basal diet that would interfere with the conduct of this study.

8. Water: Tap water, ad libitum. Water is monitored for contaminants at periodic intervals according to FDRL Standard Operating Procedures.

9. Environment: All animals will be housed in environment-controlled rooms as per "Guide for the Care and Use of Laboratory Animals". A 12-hour light-dark cycle will be maintained.

10. Quarantine: Minimum of 5 days. During this conditioning period, the animals will be observed for any clinical signs of disease. All animals with any evidence of disease or physical abnormalities will be discarded.

E. Dosing - Dosing will be done topically as described below at a level recommended by the client or determined from an optional dose range finding study. The concentration used for induction should provoke only a weak skin irritation, if any. The positive control material will be dissolved in ethanol for the induction and in acetone for the challenge.

F. Experimental Design

1. Daily observations will be recorded for all animals noting appetite, elimination, general appearance and behavior, gross signs of toxic effects and mortality. A gross necropsy will be performed on all animals that die during the course of the study.

2. At the termination of the study, all animals will be sacrificed by exposure to CO₂ gas and then discarded.

INDUCTION OF CONTACT SENSITIZATION

1. The left dorsal surface of 10 test group guinea pigs and 6 guinea pigs per control group will be shaved with electric clippers.
2. Day 1: The test article, positive control and/or vehicle will each be topically applied to the shaved area of the appropriate guinea pigs.
3. The volume of each material used will be 0.5 ml or 0.5 g.
4. Animals will be treated topically and a 2 x 2 cm gauze patch applied to the application site on each animal. The sites are then occluded using Micropore® tape and an occlusive binder according to FDRL Standard Operating Procedures. The binder and patches will be removed after 6 hours and any remaining test article gently wiped with a clean gauze.
5. This procedure, consisting of topical exposure and occlusive binding will be performed again on days 8 and 15 along the shaved area of the left dorsal surface choosing a new location for each treatment.
6. Dermal irritation readings for erythema, eschar formation and edema according to the method of Draize (1965) will be taken 24 and 48 hours after each application of the test article (see Attachment 1 for Draize scoring method).

ELICITATION OF CONTACT SENSITIVITY

1. Day 28: The right dorsal surface of all guinea pigs will be shaved over the right flank to expose a virgin site.
2. Day 29: The guinea pigs in the test article, positive control and/or vehicle control groups will each receive a topical application of 0.5 ml or 0.5 g of the appropriate material and 0.5 ml of the respective vehicle applied to separate virgin sites. The 3 additional naive animals will receive the test article as well.

3. A 2 x 2 cm gauze patch will be applied over each application site on each animal. The sites will then be occluded using Micropore® tape and an occlusive binder according to FDRL Standard Operating Procedures.
4. The binders and patches will be removed after 6 hours. Dermal irritation readings will then be taken at 24 and 48 hours post-application.
5. Animals will be rechallenged if a questionable response is noted at the first challenge.

G. Analysis of Data - The dermal sensitization potential of the test article will be determined by comparing erythema and edema scores obtained 24 and 48 hours after the first sensitizing dose with those obtained after the challenge dose using an extension of the Mantel-Haenszel Procedure (Mantel, 1963). If other statistical procedures are employed, they will be documented in the final report.

H. Report - One copy of the draft report and two copies of the final report will be submitted to the Sponsor. The final report will contain a description of the experimental design, observations, individual and summary skin score data by group and an estimate of the sensitizing potential of the test article.

I. Retention of Data - All data including reports from this study will be retained in accordance with the pertinent government regulations. In any case, the Sponsor will be contacted prior to disposition of these materials.

J. Compliance with Government Regulations - The study will be conducted according to the Good Laboratory Practice regulations as described by the FDA in 21 CFR Part 58 and

and FDRL Standard Operating Procedures. Changes in the protocol will not be made without the specific written request or consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such change will be honored by FDRL. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification. If departure otherwise occurs from this protocol or the GLP regulations, this will immediately be brought to the attention of the Sponsor.

K. Quality Assurance - This study will be inspected and the final report reviewed by FDRL's Quality Assurance Section in accordance with FDRL's Standard Operating Procedures along with the pertinent government regulations.

L. References

- Buehler, E.V. and Griffith, F., Experimental skin sensitization in the guinea pig and man. In: Animal Models in Dermatology. H.I. Maibach (ed.), Churchill Livingstone, Edinburgh. pp. 56-66, 1975.
- Draize, J.H., Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. Association of Food and Drug Officials of the United States, Topeka, Kansas, 1965.
- Magnusson, B. and Kligman, A.M., Allergic contact dermatitis in the guinea pig. Identification of contact allergens. Thomas, Springfield, Illinois, 1970.
- Mantel, N., Chi-square tests with one degree of freedom; extensions of the Mantel-Haenszel Procedure., J. Amer. Stat. Assoc., 58:690-700, 1963.

Attachment 1

Value

Erythema and eschar formation:

No erythema.	0
Very slight erythema (barely perceptible). . .	1
Well-defined erythema.	2
Moderate to severe erythema.	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth) . . .	4

Edema formation:

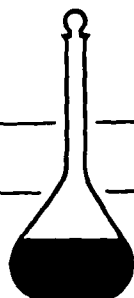
No edema	0
Very slight edema (barely perceptible) . . .	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm) .	3
Severe edema (raised more than 1 mm and extending beyond the area of exposure) . .	4

APPENDIX C
EYE IRRITATION STUDY

NAS 9-17428 - EL 04-85-GC1

A Study To Define A Set of Requirements
For Cleansing Agents For Use In The Space Station
Whole Body Shower

October 29, 1985

DRAFT COPY**Hill Top Research, Inc.***P.O. Box 42501, Cincinnati, Ohio 45242 (513) 831-3114*

85-1469

October 1, 1985

EYE IRRITATION STUDY**For: Economics Laboratories, Inc.****OBJECTIVE**

To compare the test material for eye irritation potential.

INVESTIGATOR

Organization: Hill Top Research, Inc
Investigator:
Location: Miamiville, Ohio 45147

STUDY DESIGN

This study is a controlled, double-blind randomized non-crossover study involving ten (10) subjects and comparing the test material to physiological saline solution (or suitable control).

STUDY POPULATION

These may be males and females between the ages of 18 and 50. Women with childbearing potential may be included. Persons who normally wear contact lenses may be included, although they will not wear their lenses on the day of the study or until completion of the study.

Exclusions:

1. Persons who have used the following systemic or ophthalmic drugs in the week prior to the study:
 - a) Antihistamines
 - b) Corticosteroids
 - c) Sympathomimetics or other vasoconstrictors
2. Persons with known ocular disease such as infection, glaucoma, cataract, retinal detachment, etc.
3. Persons with evidence of eye irritation at the pre-treatment examination.



85-1469

October 1, 1985

-2-

DRAFT COPYExclusions (continued):

4. Persons who have participated in an ocular irritation study within the previous 48 hours.
5. Persons who have not complied with the pre-test instructions.
6. Persons who are unsatisfactory subjects in the opinion of the investigator.

STUDY PROCEDURE

The volunteers will be recruited at least seven days prior to the study. They will be instructed to follow the four rules given on the attached instruction sheet (Exhibit A).

Prior to the study, the volunteer's eyes will be examined for the degree of redness of the conjunctival surface of the eye and the inner surface of the lower eye lid.

Ten volunteers selected for the study will give informed consent prior to participation (See Exhibit B).

TEST MATERIALS

Test materials and diluents:

<u>Sponsor's Sample Code</u>	<u>Hill Top Research Code</u>	<u>Physical Description</u>	<u>To Be Tested As (Concentration)</u>
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

The sponsor will provide the investigator with a summary of the following:

- 1) Acute rabbit eye irritation tests of test material
- 2) Sterility tests - test material and diluent
- 3) pH determinations - test material and diluent

Labels for each container will indicate the identity, strength, volume, control number, name of sponsor, and the legend "Warm to 37°C prior to testing".

After dilution and mixing, no more than one hour before the study, test solutions will be transferred to pre-labeled 60 ml dropper bottles and warmed in a 37°C water bath. No diluted test product will be used if it is more than two hours old. Unused test samples will be returned to the sponsor at the end of the study.

85-1469

October 1, 1985

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Test Materials (Continued)**DRAFT COPY**Dosage:

One drop of assigned test solution will be placed in the inferior cul-de-sac of the assigned eye in the following sequence.

Right eye first
Left eye second

For each individual, a new sterile eye dropper will be used for each solution, then discarded.

Any excess solution that falls from the eye will be blotted with tissues, a separate tissue for each eye. The subject will then move from the treatment area to the scoring area.

Treatment Assignment:

See Exhibit C.

SCORING OF IRRITATIONSchedule:

All eyes will be examined as follows:

Pre-test
30 seconds after instillation
15 minutes after instillation
60 minutes after instillation
2 hours after instillation

The Medical Consultant will score (see Exhibit D for Scoring Scale) and shall be unaware of each subject's treatment assignment and his previous ratings. Scores will be recorded by a separate recorder.

If persistent adverse reactions are present at the 2-hour examination, the subject will remain for examination at 4 hours following instillation. If adverse reactions are still present at the 4-hour examination the subject will return for re-examination at 24-hour intervals until the eyes have returned to normal.

Submitted for: Hill Top Research, Inc.

By: _____
John E. Wild Date

Accepted for: Economics Laboratories, Inc.

By: _____
Date

HILL TOP RESEARCH
Miamiville, Ohio

DRAFT COPY

PANELIST INSTRUCTIONS

1. In the week before the study you must not use any eye drugs, antihistamines, nasal decongestants, or cortisone type anti-inflammatory drugs.
2. Beginning two days before the study do not use eye make-up or false eyelashes.
3. On the day before and on the day of the study avoid alcoholic beverages, tobacco smoke, and excessive sun exposure.
4. If you wear contact lenses, do not use them on the day of the study.

REPORT TO HILL TOP RESEARCH AT 8:00 AM ON _____

PRE-TEST HISTORY AND EYE EXAMINATION

DRAFT COPY

SUBJECT NO. _____ DATE _____
 PANELIST'S INITIALS _____ AGE _____ SEX _____ RACE _____

Please answer the following questions "Yes" or "No".	<u>Yes</u>	<u>No</u>
Do you usually wear contact lenses?	—	—
If yes, did you wear them today?	—	—
Do you usually wear glasses?	—	—
In the past two days have you used any eye drug, or taken antihistamines, nasal decongestants, or cortisone-type anti-inflammatory drugs?	— —	— —
To your knowledge, do you have any eye infection, glaucoma, cataract or detached retina or other eye disease?	— —	— —

 Signature / Date

Visual Acuity at 20 feet:	<u>Right</u>	<u>Left</u>
Uncorrected	—	—
Corrected	—	—
	<u>Right</u>	<u>Left</u>
Corneas	— Clear	— Clear
Lenses	— Clear	— Clear

Comments: _____

 Signature / Date

DRAFT COPY

TREATMENT ASSIGNMENT

<u>SUBJECT NUMBER</u>	<u>PANELIST INITIALS</u>	<u>RIGHT EYE</u>	<u>LEFT EYE</u>
1	_____	_____	_____
2	_____	_____	_____
3	_____	_____	_____
4	_____	_____	_____
5	_____	_____	_____
6	_____	_____	_____
7	_____	_____	_____
8	_____	_____	_____
9	_____	_____	_____
10	_____	_____	_____

DRAFT COPY**SCORING SCALE****Sting (pain, smarting, etc.**

- 0 = within normal limits
- 1 = mild, very slight
- 2 = moderate
- 3 = severe

Lacrimation

- 0 = within normal limits
- 1 = excessive wetness (no distinct tears)
- 2 = a few formed tears (contained in orbit)
- 3 = intense tearing (leaving orbit)

Irritation**Bulbar Conjunctiva:**

- 0 = within normal limits
- 1 = mildly pink
- 2 = moderately pink, some dilation
- 3 = intense red vessels, dilated

Palpebral Conjunctiva:

- 0 = within normal limits
- 1 = mildly pink
- 2 = moderately pink
- 3 = cherry to deep red

EYE IRRITATION SCORES

DRAFT COPY

SUBJECT NO. _____ DATE _____

PANELIST'S INITIALS _____ AGE _____ RACE _____

Medication in past 7 days: ☐ None, or list name, dosage and condition being treated.

Time	Pre-Treatment		Post Treatment											
			30 Seconds		15 Minutes		1 Hour		2 Hours		Hours		Hours	
Eye (Right Left)	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Stinging														
Lachrymation														
Redness														
Bulbar Conjunctiva														
Redness Palpebral Conjunctiva														

COMMENTS: _____

ORIGINAL PAGE IS
OF POOR QUALITY_____
Scorer's Signature Date_____
Recorder's Signature Date

APPENDIX D

PROTOCOL FOR COMPARING SHAMPOOS

NAS 9-17428 - EL 04-85 - GC1

A Study To Define A Set of Requirements
For Cleansing Agents For Use in the Space Station
Whole Body Shower

October 29, 1985

DRAFT COPY

85-1380

September 18, 1985

PROTOCOL FOR COMPARING SHAMPOOS
For: Economics Laboratories

PURPOSE

To determine the relative cosmetic value and rinseability of five test shampoos in a controlled split use study.

TEST SPONSOR AND MONITOR

Economics Laboratories
Robert Hall

INVESTIGATIVE ORGANIZATION, TEST LOCATION AND PERSONNEL

Organization:	Hill Top Research, Inc.
Location:	Miamiville, Ohio
Investigator:	John E. Wild
Clinical Associate:	Thelma J. Williams
Project Leader:	_____
Beauticians:	_____

TEST MATERIALS

The sponsor will furnish the test shampoos.

PANELIST SELECTION CRITERIA

Twenty-five female panelists with short or medium length hair that has not been color treated or bleached, and who normally shampoo at home, will be enrolled for the study.

A demographic profile will be obtained at the start of the study. Panelist with known scalp disease will be excluded. Informed consent will be obtained from each panelist prior to the shampoo use.

85-1380

September 18, 1985

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PROCEDURE

A licensed beautician will shampoo each panelist using a split-use technique. One of the five test shampoos will be assigned to one side and the panelists regular shampoo (brought from home) will be used on the opposite side.

A technician will issue the shampoo to the beautician in a coded container so the beautician will be blinded as to the type of shampoo being used. The beautician will score the latherability of the shampoos and the technician will measure the amount of deionized water required for rinsing.

The right side of the head will always be shampooed first and then rinsed and the second shampoo will be used on the left side and rinsed.

A sample of the shampoo assignment is as follows:

<u>Group</u>	<u>Sample</u>	<u>No. of Panelists</u>	<u>Right</u>	<u>Left</u>
1	A	3	A	Panelist shampoo
		2	Panelist shampoo	A
2	B	2	B	Panelist shampoo
		3	Panelist shampoo	B
3	C	3	C	Panelist shampoo
		2	Panelist shampoo	C
4	D	2	D	Panelist shampoo
		3	Panelist shampoo	
5	E	3	E	Panelist shampoo
		2	Panelist shampoo	D

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DRAFT COPY

Immediately following the shampooing, another licensed beautician will comb the hair and score each side for ease of combing. The panelists will then dry their hair in their usual manner. The drying technique used will be recorded on the evaluation sheet. After the hair is dried, the beautician who scored the wet hair will score the dry hair for the following attributes by the scoring scale shown:

Side
R L

Ease of Combing
Static Fly
Softness
Manageability
Shine/Luster

Scoring Scale

2 - Much Better
1 - Slightly Better
0 - No Difference

Copies of the demographic profile form, the Informed Consent and the wet and dry evaluation forms are shown as Exhibit A, B, C and D, respectively.

Both beauticians will be blinded to the Sample Assignment and will dictate scores to a recorder who will enter the scores on the case report forms.

REPORT

All data and conclusions will be presented in a final project report.

Submitted for: Hill Top Research, Inc.

By: _____

John E. Sted

9/20/85
Date

Accepted for: Economics Labs

By: _____

Date

85-1380
Exhibit ADEMOGRAPHIC PROFILE

DRAFT COPY

NAME: _____ PANELIST NO. _____

AGE: _____ HAIR: Color _____
Texture _____ (Fine, medium, course)
Length _____ (short, medium)Do you use hair coloring or bleach? Yes _____ No _____
If answer is yes, panelist is not acceptable.

Do you use a blow dryer or dry hair at room temperature? _____

How often do you shampoo your hair? _____

What brand of shampoo are you now using? _____

Do you have any scalp disease such as psoriasis or seborrhea? Yes _____

No _____

If yes, panelist is not acceptable.

Interviewer's Signature / Date

INSTITUTION: Hill Top Research, Inc.
INVESTIGATOR: John E. Wild
STUDY TITLE: Hair Shampoo

85-1380 APPENDIX D
Exhibit B

INFORMED CONSENT STATEMENT

This study involves research on hair shampoo products. The study will last for 1 day. During the study, you will be asked to come into the lab for a split-use shampoo application on Day 1 of the study.

The products have been studied to safety in animals and humans. No adverse effects are anticipated.

The participants in this study are not expected to gain any major benefits from application of the test products, but the test results may allow a new or improved product to be marketed.

Hill Top Research will keep confidential information concerning you that is obtained in connection with this experiment, except that the Company whose product is being tested will receive a copy of the study. In addition, the Food and Drug Administration and others in certain legal actions may inspect the records of the study.

If, in the course of this experiment, you experience illness, discomfort or injury which appears to be a result of the experiment, Hill Top Research will provide you with medical care. Provision of such medical care is not an admission of legal responsibility.

In certain cases of illness or injury resulting from this study, workmen's compensation may be available. Pursuant to Ohio law, Hill Top Research has elected to secure workers' compensation coverage for participants in its studies and tests, and has paid and will pay appropriate premiums into the State insurance fund on behalf of such participants.

If you have any questions about this experiment or your rights in the case of side effects or injury, contact any staff member at 831-3114 who will arrange for you to meet with the Investigator or the Manager.

I understand that I will be paid an agreed upon amount for completion of this study. I know that I may drop out at any time. If I drop out on my own account for personal reasons or am dismissed for refusal to obey rules or follow directions, I will not be paid. If, in the judgment of the Investigator, it is best to discontinue my participation in the experiment for other reasons, I will either be paid in full or for that portion of test already completed.

I have read all the above information and was given an opportunity to ask questions about any part of it. Answers to such questions (if any) were satisfactory. I was also provided a copy of the Informed Consent Form for my records.

I am eighteen years of age or older and freely and without reservation give my informed consent to serve as a subject in this experiment.

PANELIST FULL NAME PRINTED _____

ADDRESS _____ CITY _____ STATE _____ ZIP _____

TELEPHONE NUMBER _____ SOCIAL SECURITY NO. _____

DO NOT WRITE BELOW DOUBLE LINE

PANELIST SIGNATURE _____ DATE _____

WITNESSED BY _____ DATE _____ PANELIST NO. _____

LATHER, RINSEABILITY AND
WET HAIR EVALUATION

(To be
completed
at end of
study.)

<u>Pan. No.</u>	<u>Lather</u>		<u>Rinseability</u>		<u>Mls. of Water Needed for Rinsing</u>		<u>Ease of Combing</u>		<u>Sample Assignment</u>	
	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>
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Recorder's
Initials _____

Scoring Scale

2 - Much Better
1 - Slightly Better
0 - No Difference

DRY HAIR EVALUATION

<u>Pan. No.</u>	<u>Ease of Combing</u>		<u>Static Fly</u>		<u>Softness</u>		<u>Manageability</u>		<u>Shine/Luster</u>		<u>Overall Preference</u>	
	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>	<u>R</u>	<u>L</u>
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Recorder's
Initials _____

Scoring Scale

- 2 - Much Better
- 1 - Slightly Better
- 0 - No Difference

APPENDIX E

DETERGENT FILMING BUILD UP STUDY

NAS 9-17428 - EL 04-85-GC1

A Study To Define A Set of Requirements
For Cleansing Agents For Use In The Space Station
Whole Body Shower

October 29, 1985

DETERGENT FILMING BUILDUP STUDY

Equipment Required

Filming apparatus
Convection oven at 205°C
Analytical balance
4 - 600 mls. glass beakers
4 - 3" x 5" 316 stainless steel panels
4 - stainless steel hooks
500 ml. volumetric flasks
400 ml. graduated cylinder

Procedure

1. Wash stainless steel panels with detergent and water. Rinse with acetone.
2. Dry in 205°C convection oven for 2 hours.
3. Cool to room temperature.
4. Weigh on analytical balance.
5. Prepare solutions in 500 ml. volumetric.
6. Measure 400 ml. of each solution with graduate. Pour into beakers.
7. Hook stainless steel panels to filming apparatus.
8. Start apparatus. Let run 5 hours.
9. Dry panels in oven at 40°C overnight.
10. Remove from oven, cool to room temperature. Reweigh on the analytical balance.

Formula For Artificial Sebum

Linoleic Acid	5%
Olive Oil	20%
Coconut Oil	15%
Palmitic Acid	10%
Stearic Acid	5%
Oleic Acid	10%
Paraffin Wax	10%
Squalene	5%
Spermaceti	15%
Cholesterol	5%

Preparation of Sebum Solution

Melt sebum over steam cone.

Make 10% artificial sebum/90%

Isopropyl alcohol solution with heat and agitation.

Economics Laboratory, Inc.
Osborn Building
St. Paul, Minnesota 55102

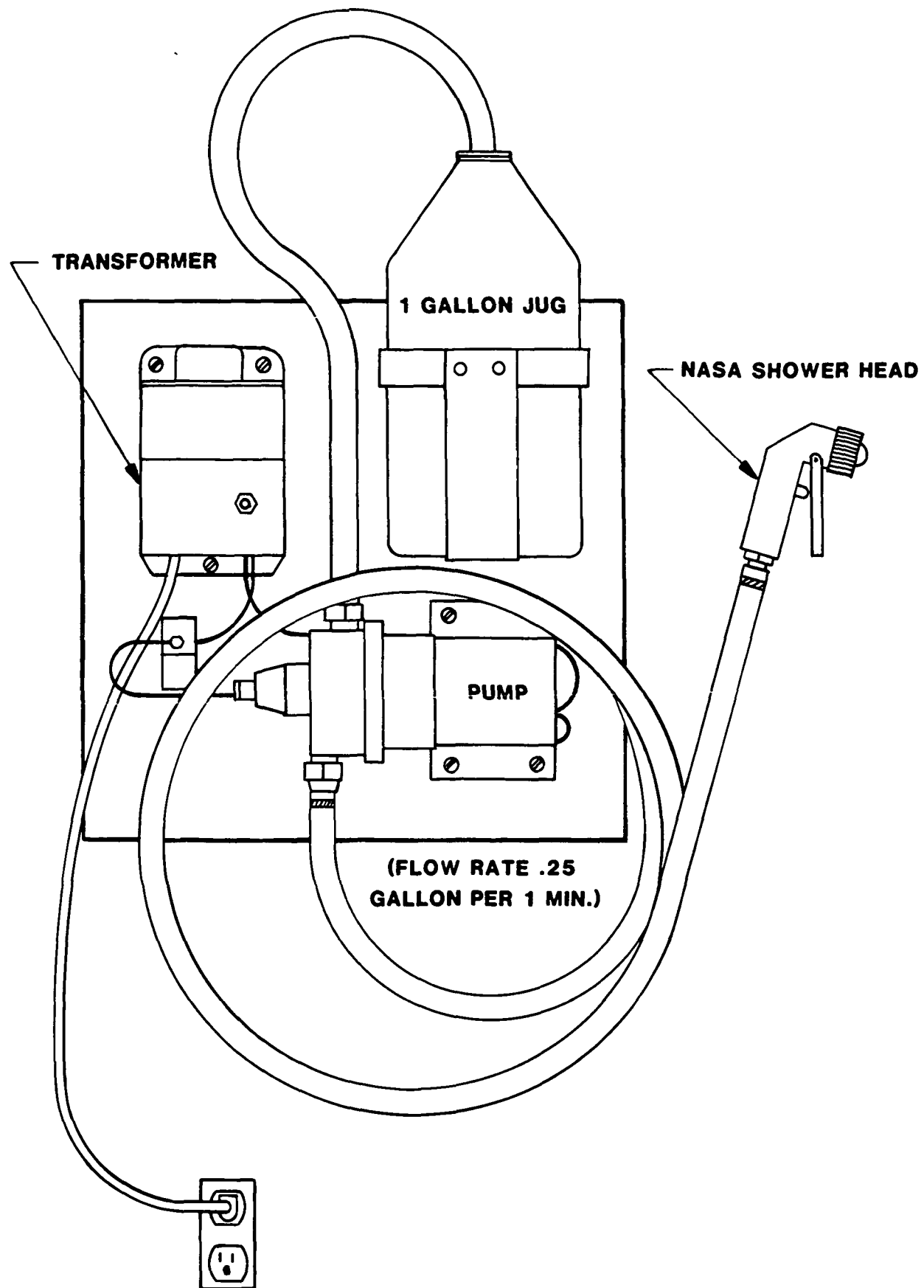


FIGURE 1. WHOLE BODY PORTABLE SHOWER HEAD UNIT